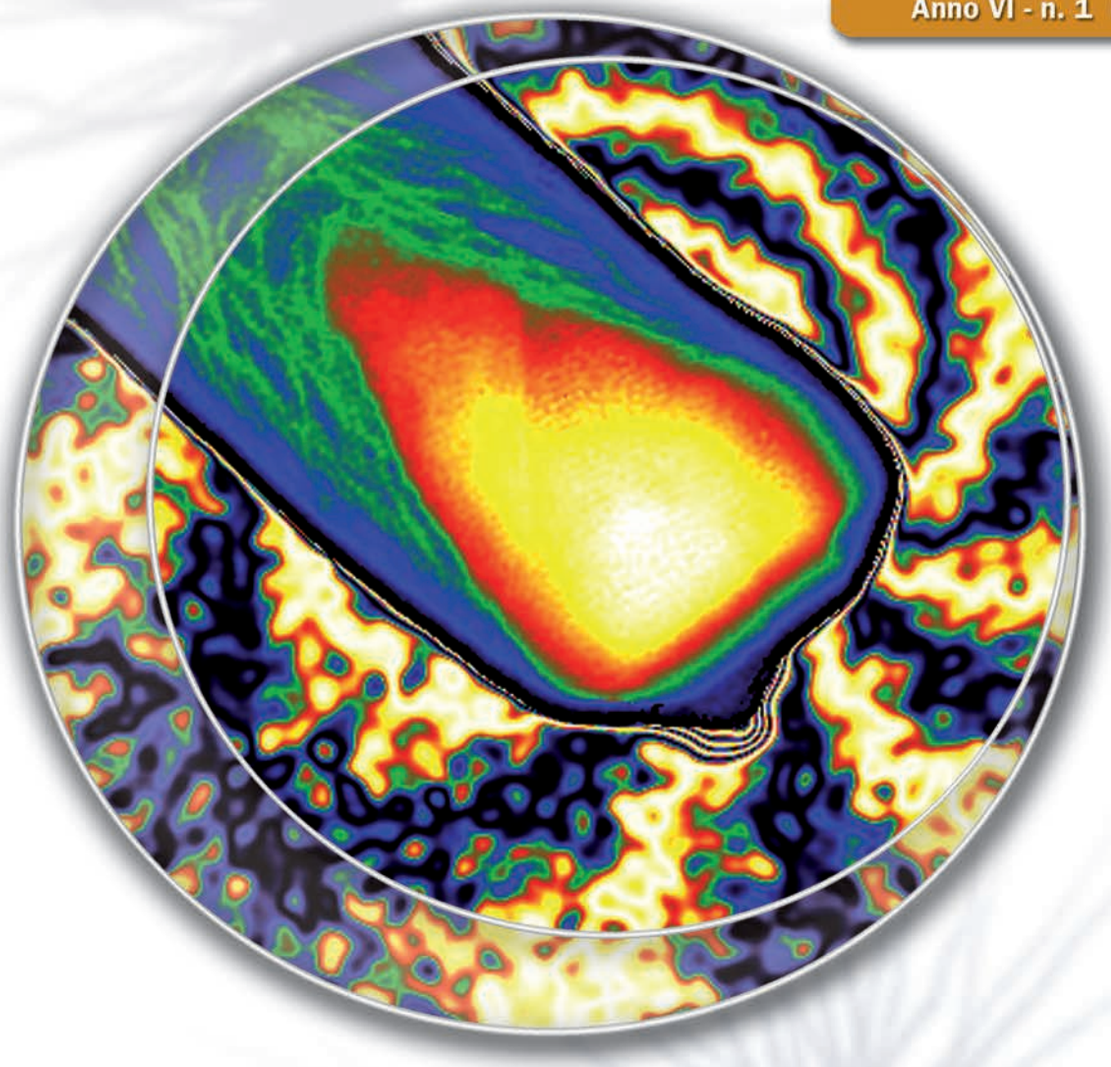
microscopie

Anno VI - n. 1 (11) - Marzo 2009



Vincitori del concorso "In copertina su Microscopie"

Attività SISM 2009

Premio "Carla Milanesi"
e Contributi di partecipazione alla MC 2009

Articolo di P.W. Hawkes

Consorzio M.I.A. (Università di Milano - Bicocca)

Società Italiana
Scienze Microscopiche

www.sism.it

Organo Ufficiale della Società Italiana Scienze Microscopiche
http://www.sism.it

Direttore Responsabile
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Comitato di Redazione
Consiglio Direttivo della Società Italiana Scienze Microscopiche

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Aut. Trib. n. 688 S.P. del 26 marzo 2008

In copertina: Linee di flusso del campo magnetico associate ad un nano-cristallo di Nickel all'estremità di una nano-fibra di Carbonio.
Immagine ottenuta tramite Olografia Elettronica
di Marco Beleggia (coautori M.A. Schofield, Y. Zhu)

Indice

ISCRIZIONE

Possono iscriversi alla Società i ricercatori e gli operatori professionali comunque attivi nel campo delle diverse microscopie. Per l'iscrizione alla Società è necessario compilare la richiesta di associazione ed inviarla al Presidente. La scheda di associazione può essere compilata direttamente sul sito web della società all'indirizzo www.sism.it oppure può essere reperita in questo periodico ed inviata via fax. Le richieste verranno valutate dal Consiglio DIrettivo nella prima riunione utile e l'approvazione dei nuovi Soci sarà comunicata personalmente agli interessati. Dopo tale comunicazione il nuovo socio può procedere al pagamento della quota sociale secondo le modalità riportate sotto.

QUOTA SOCIALE

La quota sociale è di € 35 per i soci ordinari e di € 25 per i non strutturati. I soci non strutturati, unitamente alla quota sociale, dovranno far pervenire al Presidente della Società una dichiarazione attestante il proprio status.
Modalità di pagamento:

a) mediante carta di credito dal sito www.sism.it
b) mediante invio di un assegno bancario non trasferibile intestato a S.I.S.M.
l'assegno deve essere spedito alla Dott.ssa Amelia Montone, ENEA, Dipartimento Tecnologie Fisiche e Nuovi Materiali, C.R. Casaccia, Via Anguillarese, 301 - 00123 Roma
c) mediante bonifico bancario intestato a S.I.S.M.
codice IBAN IT44V0100538880000000023074
Presso BNL-Anguillara S.
Causale: "NOME del SOCIO"

SEDE SOCIALE

Dott.ssa Amelia Montone
ENEA, Dipartimento Tecnologie Fisiche e Nuovi Materiali
C.R. Casaccia, Via Anguillarese 301, 00123 Roma
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SOCIETÀ ITALIANA SCIENZE MICROSCOPICHE

Richiesta di associazione

Si ricorda che le richieste di associazione verranno valutate dal Consiglio Direttivo e l'approvazione dei nuovi Soci verrà comunicata personalmente agli interessati.
Il pagamento della quota di associazione deve essere effettuato solo dopo il ricevimento della comunicazione dell'approvazione, da parte del Direttivo, della richiesta di associazione.

Il sottoscritto rischiede l'ammissione alla SISM in qualità di:

❑ Socio ordinario (35 euro)
❑ Socio non strutturato (25 euro)

Titolo, Nome e Cognome

Data di nascita

Titolo di studio e qualifica

Tipo di istituzione

❑ Università ❑ CNR ❑ Industria ❑ Commerciale ❑ Altro ente pubblico di ricerca

Istituto/Ente/Ditta

Dipartimento

Indirizzo

Città CAP

Telefono Fax E-mail

Indirizzo cui inviare la corrispondenza, se diverso dal precedente

Settore di attività

❑ Biomedico ❑ Scienza dei materiali ❑ Commerciale ❑ Altro (specificare) _____

Come deliberato nell'Assemblea Generale del 24/09/2001 ogni Socio SISM è anche Socio EMS.
Questi stessi dati saranno pertanto automaticamente inviati anche all'EMS, di cui la SISM fa parte. I dati dei Soci sono utilizzati dalla Segreteria EMS per distribuire il Notiziario in forma elettronica, per annunciare informazioni importanti come Congressi, Corsi, Scuole e per pubblicare l'Annuario dei Soci EMS.
Se si desidera che i propri dati personali non compaiano nell'annuario EMS, selezionare l'apposita opzione.

❑ Chiedo che il mio indirizzo privato non compaia nell'annuario EMS
❑ Chiedo che il mio numero di telefono/fax non compaia nell'annuario EMS

Data _____ Firma _____

Inviare via fax a:
Dott.ssa Amelia Montone
ENEA, Dipartimento Tecnologie Fisiche e Nuovi Materiali C.R. Casaccia, Via Anguillarese, 301 00123 Roma
Tel +39.06.30484762/4764 Fax +39.06.30483176

Editoriale

Cari Amici,

le attività della SISM del 2008 hanno avuto un grande successo grazie all'alto livello scientifico che da sempre le caratterizza e grazie alle Ditte che hanno supportato le nostre iniziative. Gli introiti della Società hanno permesso, tra l'altro, di bandire, per i giovani, Contributi di Partecipazione ed il Premio "Carla Milanesi" per la Microscopy Conference 2009, che si terrà a Graz, in Austria, dal 30 Agosto al 4 settembre 2009.
Per il 2009 sono previsti il Congresso biennale della SISM e l'assemblea ordinaria dei soci SISM che si svolgeranno all'interno del MC 2009. Durante l'assemblea avverrà la designazione dei candidati per il rinnovo del Consiglio Direttivo; ricordo che solo chi è in regola con le quote associative ha diritto alle candidature ed alle votazioni che seguiranno.
In occasione dell'assemblea saranno presentate le candidature per il prossimo Congresso; ad Aachen era stata suggerita una candidatura italiana, successivamente seguita dalla proposta dell'Università di Urbino: la Prof.ssa Elisabetta Falcieri ha già ottenuto l'autorizzazione degli organi competenti e l'Ateneo ha cominciato ad organizzarsi; contiamo di essere pronti a Graz per presentare la nostra proposta!
La registrazione e la sottomissione degli abstract al MC 2009 sono state aperte il 15 gennaio 2009; vi anticipo, inoltre, che sono stati invitati molti italiani come *chairpersons* su proposta del Programme Committee.
Per quanto riguarda le iniziative nazionali della SISM per il 2009, quest'anno, tenendo conto delle esigenze dei Soci che ci hanno contattato, organizzeremo una Giornata di Studio "Metodi di Nanoscopia ottica" a Genova, una "Scuola teorico-pratica di Microscopia Elettronica a Scansione applicata ai materiali nanostrutturati" a Roma, ENEA C.R. Casaccia, ed un Corso teorico-pratico "Tecnica ed applicazioni dei calchi vascolari (corrosion cast)" a Varese.
Quest'anno sulla copertina della Rivista saranno pubblicate le foto vincitrici del Concorso "In copertina su Microscopie"; la scelta dei vincitori è stata difficile, tutte le immagini inviate erano da pubblicare!
In questo numero di Microscopie sono stati pubblicati i lavori dei vincitori del Premio SISM 2008; anche stavolta, come potrete vedere, abbiamo avuto il piacere di premiare giovani ricercatori di eccellente livello.
Al momento sono pochi i Soci in regola con il pagamento delle quote associative, vi ricordo che i Soci morosi da oltre due anni sono considerati decaduti dalla Società e questo comporta non solo la cancellazione dall'elenco dei Soci SISM, ma anche dall'elenco dei Soci EMS, vi prego quindi di mettervi in regola al più presto per continuare ad essere parte attiva della SISM.
Vi aspetto a Graz!
Buon lavoro!

Amelia Montone

Editoriale

Cari Soci,

siamo giunti al nostro secondo appuntamento editoriale: la gestione dei due numeri di Microscopie del 2008 hanno rappresentato per me un'esperienza nuova ed il completamento di ogni fascicolo è diventato una ricorrente fonte di soddisfazione: mi sento di rivolgere, ancora una volta, un doveroso grazie a tutti quei Soci che hanno reso possibile la realizzazione della Rivista ed un invito, sincero e caloroso, a tutti Voi perché collaboriate a riempire di notizie, informazioni e contributi scientifici i prossimi numeri.
Quest'anno si apre con una novità: grazie al concorso "In copertina su Microscopie" vedremo pubblicate sulla copertina dei due fascicoli del 2009 due immagini originali (una inerente le Scienze dei Materiali, l'altra le Scienze Biomediche) scelte dal Consiglio Direttivo, su base puramente estetica, tra le numerose proposte da nostri giovani Soci. Potrebbe sembrare una iniziativa un poco al di fuori degli scopi di una rivista scientifica, ma credo che il nostro compito sia quello di promuovere la microscopia sotto ogni aspetto, non limitandoci alla "sola" valenza scientifica.
Le immagini rappresentano, per noi microscopisti, il frutto delle nostre fatiche e la prova del risultato scientifico ma, di tanto in tanto, è bello dimenticare il nostro bagaglio culturale e provare a godere della loro sola bellezza, lasciandoci guidare dalla sensazione di meraviglia che certe combinazioni di forme e colori riescono a suscitare nel nostro animo.
Il mio primo incontro con questo modo di guardare le immagini scientifiche, tanto lontano dalla mia formazione e consuetudine professionale, risale a molti anni fa. A quei tempi mia sorella frequentava l'Accademia delle Belle Arti e, alla ricerca di nuove idee per il corso di Tecniche Pittoriche, mi chiese di consultare il mio archivio di fotografie di microscopia elettronica a trasmissione: si trattava di campioni di diversi tessuti biologici ma Monica, ignorando il loro significato scientifico, riuscì ad intravvedervi figure fantastiche, che rese evidenti con uno smalto rosso trasparente. Quelle fotografie (che le valsero un bel trenta e lode!) sono appese da dieci anni nel mio studio e suscitano l'interesse e, talora, l'ammirazione di chi le osserva, rammentando a me ogni giorno quanto bella possa essere, di per sé, un'immagine microscopica.
Oggi, l'avvento del digitale ha reso tutto il nostro lavoro più semplice, i programmi di gestione delle immagini consentono di sperimentare rapidamente e con poca fatica le più svariate trasformazioni grafiche, ottenendo spesso risultati spettacolari. Forse è proprio per questo che, da qualche tempo, sono in atto varie iniziative volte alla valorizzazione artistica delle immagini scientifiche.
Ne è prova l'interessante progetto, descritto in questo numero della rivista, che il Consorzio M.I.A. dell'Università di Milano-Bicocca sta portando avanti in collaborazione con le scuole medie superiori e, in particolare, con i Licei artistici, per far conoscere ai giovani il mondo della microscopia in tutti i suoi molteplici aspetti.
Questo numero di Microscopie contiene anche un'altra importante novità: nella sezione "Notizie", a pagina 18, troverete la fedele riproduzione di un articolo recentemente pubblicato sulla rivista Ultramicroscopy e scritto dal Dott. Peter W. Hawkes, esperto di

fisica, ottica e microscopia elettronica di fama internazionale, ex direttore del Laboratoire d'Optique Electronique (CEMES) di Toulouse (Francia) ed emerito del CNRS. In questo articolo, il Dott. Hawkes commenta il libro "1956-2006. Cinquanta anni di microscopia in Italia tra storia, progresso ed innovazione", pubblicato dalla nostra Società nel 2006 per celebrare l'anniversario della fondazione della SIME (ora SISM), esprimendo vivo apprezzamento per gli articoli in esso contenuti e lodando l'iniziativa della Società. Il Dott. Hawkes dedica anche un affettuoso ricordo al nostro compianto Piergiorgio Merli, rendendogli merito delle sue qualità umane e professionali. Questo articolo rappresenta quindi un riconoscimento in campo internazionale degli sforzi compiuti dalla nostra società per diffondere e valorizzare le scienze microscopiche e un omaggio alla memoria di Piergiorgio Merli, che testimonia una volta di più la grande considerazione di cui godeva nel mondo scientifico.
Mi auguro che questo riconoscimento sia di stimolo a tutti noi nel fornire un contributo – di idee e di impegno lavorativo – affinché la nostra Società continui ad essere prodiga di iniziative culturali per le quali Microscopie, grazie alla sua ampia diffusione, costituirà sempre un efficiente mezzo di divulgazione.

Manuela Malatesta

Consiglio direttivo della SISM

Verbale della riunione del 14 luglio 2008

Università di Bologna, Dipartimento di Scienze Anatomiche Umane, via Irnerio, 48

Il giorno 14 luglio 2008 alle ore 11 presso il Dipartimento di Scienze Anatomiche Umane in Via Irnerio 48, a Bologna, si riunisce il Consiglio Direttivo della Società Italiana di Scienze Microscopiche, per discutere il seguente ordine del giorno:

1. Approvazione del verbale della riunione precedente

2. Situazione economica della Società

3. Premio SISM 2008

4. Attività SISM 2008 e proposte attività 2009

5. EMC2008, MC2009 e proposte candidature per i prossimi Congressi

6. Preparazione del prossimo numero della Rivista

7. Sito web

8. Approvazione ammissione nuovi Soci

9. Varie ed eventuali.

Sono presenti: *Roberto Balboni*, *Elisabetta Falcieri*, *Guido Macchiarelli*, *Manuela Malatesta e Amelia Montone*.
Assenti giustificati: *Alberto Diaspro e Mario Raspanti*.
Presiede *Amelia Montone*; svolge le funzioni di segretario verbalizzante *Roberto Balboni*.

1. Il verbale della riunione del Direttivo del 10 Marzo 2008 viene approvato all'unanimità.
2. Il Presidente illustra il bilancio non ancora definitivo delle scuole di Genova e di Napoli, comunica le entrate dovute alle Ditte che hanno sponsorizzato gli eventi SISM e le uscite effettuate: queste ultime comprendono la quota IFSM (International Federation of Societies for Microscopy) ed il compenso alla tipografia PIME per la stampa della rivista.
3. Per stilare la graduatoria, secondo quanto stabilito dal bando, sono stati considerati:
   1. Interesse ed originalità del contributo inviato (valorizzando chi ne ha presentato più d'uno).
   2. Curriculum vitae (valorizzando eventuali esperienze all'estero).
   3. Qualità e numero delle pubblicazioni scientifiche inerenti alle tematiche di microscopia.

   Si è tenuto conto, ove necessario, dell'eventuale iscrizione alla SISM.
   Il CD ha approvato la seguente graduatoria:

   Settore Materiali
   1. Grillo Vincenzo
   2. Albonetti Cristiano
   3. Felisari Laura
   4. Mirabile Gattia Daniele e Aurora Annalisa
   5. Ortolani Luca

Settore Biologico
1. Battistelli Michela
2. Cisterna Barbara
3. Spedito Alessandro
4. Santin Giada

Il Dr. Grillo e la Dr.ssa Battistelli risultano pertanto vincitori di una borsa per la partecipazione al 14° EMC che si terrà ad Aachen dal 1 al 5 settembre 2008.
Visto quanto stabilito nel bando, viene assegnato il premio di due anni gratuiti di iscrizione alla società a tutti i candidati.

4. Il Presidente relaziona sull'attività svolta fino ad ora nell'anno 2008.
   - Giornata di Studio "Aspetti pratici di Microscopia Multifotonica e Nanoscopia"
     Genova, 3 giugno 2008
     5 iscritti
   - Corso teorico-pratico SISM " Tecniche di microscopia elettronica a trasmissione: dalla morfologia alla biologia molecolare *in situ*"
     Napoli, Istituto di Genetica e Biofisica "A. Buzzati-Traverso", CNR, 19-20 giugno 2008
     Sono state accolte 22 domande di partecipazione a fronte di un numero maggiore di richieste.

   Attività già programmate in via di realizzazione:
   - Corso teorico-pratico "Tecniche fluorimetriche e di imaging per lo studio di pellicole pittoriche, a fini conservativi."
     Pavia, 15-16 settembre 2008
     La brochure del Corso è disponibile sul sito della società.
   - Corso teorico-pratico di Microscopia Elettronica a Scansione applicata ai Beni Culturali
     Roma, Istituto Centrale del Restauro, 8-10 ottobre 2008
   - Corso teorico-pratico SISM di "Tecnica ed applicazioni dei calchi vascolari (corrosion cast)"
     Varese, previsto per fine ottobre o inizio novembre 2008
   - Scuola teorico-pratica SISM di "Microscopia a fluorescenza, confocale e multifotone"
     Genova, 15-18 dicembre 2008

   Si apre quindi la discussione sulle proposte di attività per l'anno 2009.
   Il Presidente rileva che da tempo non viene effettuato un corso sulle microscopie a sonda.
   Nel campo scienza dei materiali potrebbe essere organizzata una scuola SEM; possibili sedi possono essere Modena, Bologna o Roma (Casaccia).
   Nel campo delle scienze biologiche vengono fatte diverse proposte da verificare.
   Si decide di definire le attività SISM durante il prossimo Direttivo.

5. Il Presidente comunica le scadenze per EMC2008 ad Aachen. Ad agosto 2008 sarà disponibile il programma definitivo.
   In base al numero di iscritti alla società, la SISM è stata invitata a nominare due rappresentanti alla riunione del Consiglio generale EMS, che si terrà ad Aachen in occasione del congresso. Il CD nomina all'unanimità Amelia Montone ed Elisabetta Falcieri.
   Il Presidente comunica che il Multinational Congress 2009 si terrà a Graaz dal 30 agosto al 4 settembre 2009. Il Consiglio avvia una discussione sull'eventuale proposta italiana per l'organizzazione del Multinational Congress 2011. Elisabetta Falcieri avanza la proposta di poterlo organizzare ad Urbino.
   Il consiglio decide di acquisire ulteriori informazioni su questa possibilità, in particolare riguardo alla possibilità di ospitare un numero sufficiente di partecipanti e alla disponibilità di trasporti.

6. La rivista includerà le relazioni sui corsi tenuti a Napoli e Genova.
   Vengono approvati dal CD tutti i contenuti della Rivista.

7. Devono essere aggiornate sul sito web le pagine di descrizione ed iscrizione alle attività e corsi SISM. Il CD chiede di provvedere al più presto alla migrazione del sito web presso un provider on-line.

8. Il Consiglio approva l'ammissione alla società dei seguenti soci:
   Dr. Traini Tonino
   Dr. Albonetti Cristiano
   Dr.ssa Carangi Rosa
   Dr.ssa Cervasio Maria Rosaria
   Sig. Danieli Giovanni
   Dr.ssa De Santo Maria Penelope
   Dr.ssa Muolo Mariagrazia
   Dr.ssa Russo Valeria
   Dr.ssa Santin Giada
   Sig. Vanoni Christian

9. Nulla da discutere

Alle ore 14, null'altro essendovi da deliberare, il Presidente dichiara chiusa la seduta.

Amelia Montone
Roberto Balboni
Elisabetta Falcieri
Guido Macchiarelli
Manuela Malatesta

Bilancio esercizio 2007

Ditta 14606 SOCIETA' ITALIANA SCIENZE MICROSCOPICHE S.I.S.M.
VIA CAMPI, 287
41100 MODENA MO

Bilancio esercizio 2007
Valuta Euro
Data 15/05/2008
Pagina 1

STATO PATRIMONIALE

ATTIVITA'

Conto	Descrizione	Importo
233.4	Elaboratori	1.044,00
233	**ATTREZZATURE INDUSTRIALI E CO**	**1.044,00**
321.1	Fatture da emettere a clienti	41,31
321	**FATTURE DA EMETTERE**	**41,31**
411	**CLIENTI**	**575,00**
429.2	Depositi cauzionali vari	79,53
429	**CREDITI VARI**	**79,53**
531.6	Erario c/liquidazione Iva	1.473,84
531	**ERARIO C/IVA**	**1.473,84**
535.4	Erario c/acconto IRPEG/IRES	1.702,00
535	**ERARIO C/RIT. SUBITE E CREDIT**	**1.702,00**
571.3	CARISBO - SAN PAOLO IMI C/C 1	18.062,64
571	**BANCHE C/C**	**18.062,64**
581.3	Cassa contanti	341,54
581	**CASSA**	**341,54**
	TOTALE ATTIVITA'	**23.319,86**
	Perdita del periodo	2.061,42
	TOTALE A PAREGGIO	**25.381,28**

PASSIVITA'

Conto	Descrizione	Importo
111.1	Capitale sociale	298,43
111	**CAPITALE E RISERVE**	**298,43**
115.6	Avanzi esercizi precedenti	13.391,79
115	**RISULTATI PORTATI A NUOVO**	**13.391,79**
333.1	Ratei passivi	7.631,17
333	**RATEI E RISCONTI PASSIVI**	**7.631,17**
451	**FORNITORI**	**650,00**
469.4	Debiti diversi	2.050,89
469	**DEBITI VARI**	**2.050,89**
533.3	Erario c/rit.su redditi lav.	1.359,00
533	**ERARIO C/SOSTITUTO D'IMPOSTA**	**1.359,00**
	TOTALE PASSIVITA'	**25.381,28**

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VIA CAMPI, 287
41100 MODENA MO

Bilancio esercizio 2007
Valuta Euro
Data 15/05/2008
Pagina 2

CONTO ECONOMICO

COSTI

Conto	Descrizione	Importo
727.15	Canoni vari e licenze d'uso	42,00
727	**LOCAZIONI E CANONI**	**42,00**
733.11	Prestazioni di lavoro auton.	3.000,00
733	**PRESTAZIONI TERZI INERENTI L'**	**3.000,00**
735.1	Consulenze fiscali	7.710,56
735.4	Contributi Cassa Previdenza	308,42
735	**COSTI SERVIZI E CONSULENZE NO**	**8.018,98**
736.3	Rimborsi spese collab./ammini	1.647,28
736	**COLLABORAZIONI COORDINATE E C**	**1.647,28**
741.6	Fiere, mostre e convegni	3.254,77
741.13	Spese di viaggio	76,00
741.14	Spese per alberghi e ristoran	925,00
741	**SPESE COMMERCIALI E DI VIAGGI**	**4.255,77**
742.1	Cancelleria varia	173,84
742.3	Spese postali	457,55
742.8	Valori bollati	29,24
742	**SPESE AMMINISTRATIVE**	**660,63**
743.6	Contributi associativi	1.723,02
743.7	Abbonamenti, libri e pubblica	6.687,36
743.10	Spese varie non documentate	10,50
743.12	Spese per studi e ricerche	1.200,00
743.14	Erogazione borse di studio	1.000,00
743	**SPESE GENERALI**	**10.620,88**
746.5	Imposta di bollo e concession	73,80
746.8	Imposte e tasse deducibili	516,46
746.9	Imposte e tasse indeducibili	421,00
746	**ONERI TRIBUTARI**	**1.011,26**
747.15	Sopravvenienze passive gestio	135,00
747	**ALTRI COSTI DI ESERCIZIO**	**135,00**
761.5	Commissioni e spese bancarie	216,42
761	**ONERI FINANZIARI VERSO BANCHE**	**216,42**
763.8	Interessi passivi versam.iva	21,11
763.10	Interessi passivi da regolari	3,56
763	**ONERI FINANZIARI DIVERSI**	**24,67**
780.15	Canoni noleggio autovetture i	1.844,76
780	**ESERCIZIO AUTOVETTURE IMPRESA**	**1.844,76**

RICAVI

Conto	Descrizione	Importo
617.18	Compensi promozionali	14.200,00
617.19	Quote corsi e convegni	10.540,00
617.24	Quote associative	4.405,00
617	**RICAVI DA PRESTAZIONI**	**29.145,00**
667.5	Interessi attivi bancari	271,23
667	**PROVENTI FINANZIARI VARI**	**271,23**

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41100 MODENA MO

Bilancio esercizio 2007
Valuta Euro
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Pagina 3

C O N T O E C O N O M I C O

COSTI			RICAVI		
Conto	Descrizione	Importo	Conto	Descrizione	Importo
	TOTALE COSTI	**31.477,65**		**TOTALE RICAVI**	**29.416,23**
				Perdita del periodo	2.061,42
				TOTALE A PAREGGIO	**31.477,65**

Resoconto del Corso SISM

Corso teorico-pratico di Microscopia Elettronica a Scansione applicata ai Beni Culturali

8-10 ottobre 2008, Roma, Istituto Superiore per la Conservazione ed il Restauro

Comitato scientifico: A. Montone (CR ENEA Casaccia), M. Bartolini (ISCR), G. Guida (ISCR), G. Sidoti (ISCR)

Il corso, organizzato dalla SISM in collaborazione con l'ISCR nella suggestiva cornice del Centro Storico di Roma, è stato incentrato sui principi della Microscopia Elettronica a Scansione (SEM) e le sue applicazioni nel campo della conservazione e restauro del Patrimonio Artistico. Più di 40 partecipanti hanno assistito alle lezioni teoriche e 24 anche alla parte pratica. Gli interventi hanno coperto le tematiche del Corso sia per il SEM - SEM: Struttura e funzionamento, Microanalisi a Raggi X (M. Vittori Antisari, CR ENEA Casaccia, Roma); SEM: Tipi di segnali, Imaging, (V. Morandi, IMM-CNR, Bologna) - sia per le applicazioni nel campo dei beni culturali - SEM e microanalisi a Raggi X applicati ai materiali vitrei (M.Verità, SSV, Murano (VE)); Utilizzo del SEM per lo studio di manufatti metallici antichi con finalità conoscitive e conservative (G.Ingo, ISMN-CNR, Montelibretti (RM)); Applicazioni SEM-EDS per lo studio dei dipinti su muro, su tavola e su tela (F. Talarico, ISCR, Roma); Nanotecnologie per la conservazione del materiale lapideo (M. Favaro, P.A.Vigato, ICIS-CNR, Padova); Imaging ad Ultra Alta Risoluzione per campioni non conduttivi (G.Lamedica, Assing); Nuove tecniche di indagine microinvasiva per l'analisi di reperti storico-artistico (G. Giachi, P. Pallecchi, Soprintendenza archeologica Toscana, F.Tatti, FEI Italia). Le esercitazioni pratiche, tenute da: F. Pierdominici, A. Montone, A. Aurora, D. Mirabile Gattia (CR Casaccia-ENEA) e G. Sidoti, G. Guida, M. Bartolini (ISCR), hanno permesso di conoscere le potenzialità della tecnica del SEM con l'analisi di reperti originali.

Si ringrazia l'Assing, la FEI Italia e la Jeol Italia per aver supportato questa iniziativa e per aver partecipato attivamente al Corso portando strumentazione, materiale illustrativo e presentando novità e nuove tecniche del SEM nel campo dei beni culturali.

Si ringrazia, inoltre, per l'ottima organizzazione del Corso, il Comitato organizzatore: Annalisa Aurora (CR ENEA Casaccia), Barbara Davidde (ISCR) e tutto il personale dell'ISCR per la squisita accoglienza.

Amelia Montone

Elenco delle attività promosse dalla SISM nel 2009

Si ricorda che nel 2009 è previsto il Congresso biennale della SISM, all'interno del quale non solo si svolgeranno tutti gli adempimenti di carattere societario che lo Statuto della Società prevede in tale occasione, ma rappresenta un momento di incontro dei Soci SISM ed una proficua occasione di scambi scientifici con colleghi di altre Società di Microscopia. Tale Congresso si svolge all'interno della MC 2009 (Microscopy Conference 2009: http://www.microscopy09.tugraz.at/) che si terrà a Graz in Austria dal 30 Agosto al 4 Settembre 2009.
Per favorire la partecipazione di giovani ricercatori a questo importante evento della nostra Società, la SISM, congiuntamente alle Ditte che invieranno il contributo di tipo A, ha bandito 6 Contributi di Partecipazione alla MC 2009 di € 500,00 ciascuno ed il Premio "Carla Milanesi" riservato ai due migliori contributi presentati personalmente, uno per il settore biomedico ed uno per scienza dei materiali, dell'importo di € 500,00 ciascuno.
La SISM organizzerà anche quest'anno diverse attività che per l'importanza e la attualità degli argomenti trattati, la valenza scientifica dei relatori e la possibilità di attività pratiche con strumentazioni tecnologicamente avanzate, sono rivolte a ricercatori e a personale tecnico qualificato impegnato nei diversi settori della Microscopia. Per ulteriori informazioni e per accordi sulle modalità di partecipazione (interventi, strumentazione, ecc.) si prega di contattare i direttori responsabili.

1. Giornata di Studio

Metodi di Nanoscopia ottica

Genova, 22 Settembre 2009

Il Prof. Alberto Diaspro ed i ricercatori del Centro di Ricerca del LAMBS-IFOM MicroScoBIO del Dipartimento di Fisica dell'Università di Genova saranno i docenti di questa Giornata di Studio dedicata alla Nanoscopia Ottica. Le più recenti applicazioni sulla visualizzazione delle molecole biologiche nei sistemi cellulari utilizzando interazioni ottiche lineari e non lineari saranno discusse.
Per informazioni: Prof. Alberto Diaspro (diaspro@fisica.unige.it)

2. Scuola teorico-pratica

Microscopia Elettronica a Scansione applicata ai materiali nanostrutturati

Roma, ENEA C.R. Casaccia, Ottobre 2009

La scuola, organizzata dalla SISM in collaborazione con l'ENEA, della durata di cinque (o tre) giorni, tratterà i principi della microscopia elettronica a scansione e le sue applicazioni nel campo della Scienza dei Materiali, con particolare riguardo ai materiali nanostrutturati. La Scuola, rivolta sia a ricercatori, studenti e tecnici interessati alla microscopia sia a chi opera nel campo dei materiali nanofasici, prevede una parte teorica sul SEM (elementi di ottica elettronica, interazione elettrone-materia, rivelatori e segnali, microanalisi) e sulle applicazioni innovative nel campo dei materiali nanostrutturati; una parte pratica ai microscopi elettronici a scansione (sia a pressione variabile con filamento LaB6 e microanalisi a raggi X sia FEG ad alta risoluzione) e presentazioni di novità strumentali da parte delle ditte attive nel settore.
È possibile osservare campioni portati dai partecipanti.
È previsto un test di valutazione finale per gli studenti interessati a richiedere il riconoscimento di crediti formativi universitari (CFU).
Per informazioni: Dott.ssa Amelia Montone (amelia.montone@enea.it)

3. Corso teorico-pratico

Tecnica ed applicazioni dei calchi vascolari (corrosion cast)
Varese, Novembre 2009

Il corso, che sarà articolato in due giornate e che si terrà nelle strutture dell'Università dell'Insubria a Varese, si prefigge di presentare una panoramica a 360 gradi sulle tecniche di corrosion casting ed è rivolto a studiosi e ricercatori in tutti i settori della biologia vascolare e dei processi angiogenetici. Nella prima giornata, che avrà carattere prevalentemente teorico e che prevede il contributo di numerosi esperti del settore a livello europeo, verranno affrontate in dettaglio le varianti tecniche, i materiali attualmente disponibili, le aree di ricerca più appropriate, gli artefatti caratteristici e le applicazioni informatiche al servizio di questa tecnica. La seconda giornata avrà un carattere più applicativo e sarà interamente dedicata all'osservazione pratica al SEM di corrosion casts rappresentativi della vascolarizzazione di diversi organi: derma, encefalo, rene, intestino etc.
Per informazioni: Prof. Mario Raspanti (mario.raspanti@uninsubria.it)

Bando
per l'assegnazione del
Premio "Carla Milanesi"

La SISM, in collaborazione con le Ditte del settore della Microscopia, bandisce un Premio riservato a giovani ricercatori non strutturati che siano Soci SISM o abbiano fatto domanda di associazione alla SISM entro il 31 dicembre 2008, che presentino un contributo scientifico alla MC 2009 (Microscopy Conference 2009: http://www.microscopy09.tugraz.at/).

Ai due migliori contributi presentati personalmente, uno per il settore biomedico ed uno per scienza dei materiali, verrà assegnato il

PREMIO "Carla Milanesi"

dell'importo di € 500,00 ciascuno.

I partecipanti devono essere in regola con le quote associative ed inviare:

- Copia dell'abstract inviato al Congresso

Per partecipare alla selezione del bando, che verrà effettuata a giudizio insindacabile del Consiglio Direttivo, occorre inviare la documentazione richiesta per e-mail al Presidente della SISM, Dott.ssa Amelia Montone (amelia.montone@enea.it).

I partecipanti in possesso dei requisiti necessari possono partecipare anche ai Contributi di partecipazione alla MC 2009.

La scadenza per l'invio della documentazione coincide con la data di scadenza dell'invio degli abstracts alla MC 2009.

Al ricevimento della documentazione verrà inviata una e-mail di conferma dell'avvenuta ricezione.

È fatto obbligo partecipare a tutta la durata del Convegno, pena esclusione dalla graduatoria.

I risultati della selezione verranno pubblicizzati sulla pagina web della SISM all'indirizzo: www.sism.it

Bando per l'assegnazione di Contributi di partecipazione alla **Microscopy Conference 2009**

30 agosto - 4 settembre 2009, Graz

La Società Italiana Scienze Microscopiche (SISM), in collaborazione con le Ditte del settore della Microscopia, bandisce

n. 6 CONTRIBUTI

dell'importo di € 500,00 ciascuno per favorire la partecipazione di giovani ricercatori italiani alla MC 2009 (Microscopy Conference 2009: http://www.microscopy09.tugraz.at/) che si terrà a Graz in Austria dal 30 Agosto al 4 Settembre 2009.

I Contributi di partecipazione sono riservati a giovani ricercatori di età non superiore a 35 anni (al momento della scadenza del bando).

I partecipanti devono inviare:

1) Copia dell'abstract inviato al Congresso.
2) Un Curriculum Vitae di massimo due pagine con autocertificazione della propria posizione di "non strutturato".
3) L'iscrizione alla SISM, a parità di giudizio, costituirà titolo preferenziale.

Per partecipare alla selezione del bando, che verrà effettuata a giudizio insindacabile del Consiglio Direttivo, occorre inviare la documentazione richiesta per e-mail al Presidente della SISM, Dott.ssa Amelia Montone (amelia.montone@enea.it).

I partecipanti in possesso dei requisiti necessari possono partecipare anche al Premio "Carla Milanesi".

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Vincitori del concorso "In copertina su Microscopie"

Il premio "In copertina su Microscopie", bandito lo scorso autunno ed indirizzato ai giovani Soci non strutturati della SISM, ha raccolto un buon numero di adesioni e sono pervenute alla redazione della Rivista diverse suggestive immagini, da parte di ricercatori impegnati sia nelle scienze dei materiali sia in biomedicina.

Le immagini sono state esaminate dai membri del Consiglio Direttivo che hanno espresso il loro giudizio tenendo conto soprattutto della qualità estetica; sono risultati vincitori il dottor **Marco Beleggia** (Center for Electron Nanoscopy, Technical University of Denmark) per le Scienze dei Materiali e la dottoressa **Sonia Congia** (Istituto Italiano di Tecnologia, Genova) per le Scienze Biomediche.

Sulla copertina di questo numero compare l'immagine di Marco Beleggia, mentre quella di Sonia Congia sarà pubblicata sul fascicolo di settembre: ai vincitori, che sono esonerati dal pagamento della quota sociale per il 2009, saranno inviate dieci copie del fascicolo sul quale compare la loro immagine premiata.

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The gymnasium of the mind

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1. Light

1785 J. TRUSLER Mod. Times III. 166 Lord W. wished to appoint me his literator, which office was to cull out the pith of every new publication, and retail it to him at breakfast.

(Oxford English Dictionary)

Let us begin with a celebration of *Progress in Optics*, edited since it was launched in 1961 by E. Wolf, which has reached volume 50 [1]. To mark the occasion, Wolf has collected eight essays on the history of optics, beginning with "From millisecond to attosecond laser pulses" by N. Bloembergen. Not only is this of intrinsic interest but it concludes with an arresting comment: "The understanding of the attosecond processes of soft X-ray emission and its inverse of photo-ionization can be formulated in terms of electron interferometry." Next, a fascinating account of "Conical diffraction: Hamilton's diabolical point at the heart of crystal optics" by M.V. Berry and M.R. Jeffrey. Berry has accustomed us to amazing findings in his work on optical singularities over the last few decades but this may be his finest yet. His list of 10 "reasons why conical refraction is worth revisiting" is too long to reproduce here in full, so I must extract the essence. The effect was predicted by W.R. Hamilton in 1832 (published 1837) and "was an early (perhaps the first) example of a qualitatively new phenomenon predicted by mathematical reasoning …. Prediction of qualitatively new effects by mathematics may be commonplace today but, in the 1830s, it was startling." Berry and Jeffrey then remind us that "critical refraction was the first non-trivial application of phase space" and "Its observation [by H. Lloyd, in 1837] provided powerful evidence that light is a transverse wave." "It was the first physical example of a conical intersection (diabolical point) … involving a degeneracy." It "displays a subtle interplay of ray and wave physics" and "Analysis of the theory [by Berry] led to an identification of an unexpected universal phenomenon in mathematical asymptotics." Moreover, "There are extensions … of the case studied by Hamilton and their theoretical understanding still presents challenges …. Conical diffraction is a continuing stimulus for experiments. Although the fine details of Hamilton's original phenomenon have now been observed [by Berry, Jeffrey and Lunney], predictions of new structures that appear in the presence of chirality, absorption and nonlinearity remain untested." Finally, the comment I most enjoyed "The story of conical diffraction, unfolding over 175 years, provides an edifying contrast to the current emphasis on short-term science."

The third chapter, on the particle concept of light by O. Keller, is again fascinating and, despite its title, de Broglie's work is covered in detail. This leads naturally on to P.W. Milonni's chapter on "Field quantization in optics," which takes us through the difficult areas of classical and quantum coherence theory, semi-classical radiation theory, non-classical light and quantum noise. In his Acknowledgement, Milonni refers to Wolf's "Lapidary lectures" and readers will be grateful for this lapidary guide to complex material.

"The history of near-field optics" by L. Novotny brings us close to ultramicroscopy and makes fascinating reading, for Novotny has illustrated his text with generous quotations from the early writings, notably E.H. Synge and his "prophetic letters … to Albert Einstein in 1928." Since then, the basic idea has been repeatedly re-invented and "The first experimental validation of near-field microscopy using electromagnetic radiation has been undertaken by E.A. Ash and G. Nicholls" in 1972. (This is the same E.A. Ash who attempted to put one of Scherzer's methods of correcting spherical aberration into practice.) This attempt used microwaves (10 GHz) and it was not until the 1980s that near-field microscopy at optical frequencies began, with the "optical stethoscopy" of D.W. Pohl. The final section, on "Near-field optics and antenna theory," tells us that "It might appear to be a far stretch from Franklin's lightning rod (in the 18th century) to near-field optical microscopy but, similar to an antenna or a near-field probe, the efficiency of a lightning rod is characterized by its ability to concentrate and localize electric fields."

"Light tunneling" by H.M. Nussenzveig also has some beautifully chosen quotations from the earlier literature, notably in the

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section on "The glory" (see www.philiplaven.com) of which "The first recorded observation … was made at Mount Pambamarca in the Ecuador Highlands (formerly Peru) some time between 1737 and 1739 by members of a French Academy of Sciences expedition, led by Bouguer and La Condamine, accompanied by the Spanish captain and astronomer Antonio de Ulloa, to make measurements concerning the Earth's shape. This is one of the expeditions about which Voltaire wrote his satirical couplet:

"Vous avez confirmé dans ces lieux pleins d'ennui
Ce que Newton connut sans sortir de chez lui."

What they observed, as related by Bouguer, was "… a phenomenon which must be as old as the world, but which no one seems to have observed so far …. A cloud that covered us dissolved itself and let through the rays of the rising sun …. Then each of us saw his shadow projected upon the cloud …. What seemed most remarkable to us was the appearance of a halo or glory around the head, consisting of three or four small concentric circles, very brightly colored, each of them with the same colors as the primary rainbow, with red outermost …."

The seventh chapter is by E. Wolf himself, on "The influence of Young's interference experiment on the development of statistical optics." The timing is perfect for it was in 1807 that Young's *A Course of Lectures on Natural Philosophy and the Mechanical Arts* was published. "What is, however, not generally appreciated is that experiments of this kind proved to be also of fundamental importance in the development of two modern branches of statistical optics, namely the theory of polarization and the theory of coherence of light," writes Wolf, and devotes his chapter to these topics. He first leads us through the early work of Bartholinus, Huygens, Young, Fresnel, Arago, Stokes and Verdet on polarisation and coherence and then recapitulates "modern theories" of Zernike and of course Wolf himself with L. Mandel. This brings him to the "Unification of the theories of polarization and coherence," which Wolf established in 2003 and forms a large part of Ref. [2]. Before examining this, let me just mention that the final chapter of *Progress in Optics*, by D.M. Greenberger, N. Erez, M.O. Scully, A.A. Svidzinsky and M.S. Zubairy, is concerned with "Planck, photon statistics, and Bose-Einstein condensation."

Ultramicroscopists will not need to be told that E. Wolf is (co-) author of "Born and Wolf" and of *Optical Coherence and Quantum Optics* with L. Mandel. In 2003, he made (yet) another major contribution to optics by unifying the theories of coherence and of polarization and his *Introduction to the Theory of Coherence and Polarization of Light* [2] is an elementary account of these subjects, intended for an audience that might be daunted by a fully rigorous treatment. The opening chapters cover the traditional fundamentals of coherence theory, including some less-familiar aspects such as radiation from sources of different states of coherence (Schell-model sources, for example) and scattering. The last two cover polarisation and in particular, the unified theory of polarisation and coherence. The presentation is, as always, pellucid and, a feature of all Wolf's writing, the notation is chosen with the greatest care. Highly recommended!

H. Gross has edited an enormous *Handbook of Optical Systems* in six volumes. Volume 4 is a *Survey of Optical Instruments* and its 1055 pages have been written largely by Gross himself, although F. Blechinger and B. Achtner have contributed nearly 4 of the 10 chapters [3]. This is a prodigious feat! The volume of the old *Handbuch der Physik* on *Optische Instrumente* was almost as big but the various topics were covered by different authors. The subjects covered here are: The human eye, Eyepieces, Elementary systems, Photographic lenses, Infrared systems, Zoom systems, Microscope optics, Telescopes, Lithographic projection lenses and Miscellaneous. Gross's object is not to provide "a collection or an archive of proved system data, because compilations of this type are available in electronic form today. The goal of this volume is really to demonstrate and explain to the reader the various classes of system and the most important thoughts, principles and properties, which lie behind these successful solutions." "Microscope optics" (some 183 pages long) gives a good idea of the thoroughness of the work. The first section introduces us to "the illumination and the pupil imaging [which] is important and in fact essential for the image-building process and the resolution." "Color correction" is then explained and the complete layout of various modern microscopes is described. Section 42.2 describes a host of different kinds of objective lenses, including UV lenses and objectives for fluorescence microscopy. A later section discusses "Illumination optic" [*sic* but deliberate, elsewhere we meet tube optic and collector optic], with a detailed account and very nice ray diagrams of Köhler illumination. Subsequent sections cover the stereo microscope, confocal laser scanning microscopes, and "Special aspects." A very remarkable feature of the book is the lavish use of colour throughout: virtually every line drawing (of which there are hundreds) uses colour and the only half-tones in black-and-white are those that were originally uncoloured. Before leaving this superb compilation, I cannot resist quoting from Section 43.11.3 in the chapter on telescopes. Here we learn that "The three-mirror all-reflective telescope proposed by Hallam, also known as 'Hughes Walrus', can be considered as an inverse Baker system …. The overall length is about 3.4 times the focal length, which was probably the reason to call it 'walrus'." With this gnomic remark, I move on to the next item—I really would like to know how one measures the focal length of pinnipeds.

2. Mathematical morphology

I love words, they are the quoits, the bows, the staves that furnish the gymnasium of the mind.

George Eliot

This makes a nice buffer state between photons and electrons, for mathematical morphology is a branch of image processing of interest for any image. The eighth of the biennial international symposia on mathematical morphology was held in Rio de Janeiro and 38 of the articles submitted are included in the Proceedings [4]. These are placed in eight groups: Lattice theory, Geometry and topology, Signal processing, Image processing, Connectivity, Watershed segmentation, Texture and geometrical segmentation, and Algorithms and architectures. The subject is now mature and readers are expected to be "morphologically literate," so to say; a huge amount of new or elusive material is conveniently collected in this volume. Fuzzy morphology (I. Bloch, A.T. Popov); two articles by J. Serra in the second group; levellings (K. Karantzalos et al.; P. Maragos and G. Evangelopoulos, whose initial has been *eroded* in the list of contents); C. Vachier and F. Meyer send "News from viscousland" and E. Aptoula and S. Lefèvre attack "morphological colour texture characterisation." In the longest section, Watershed segmentation, there are nine papers, including one by L.A. Morales-Hernández et al. on directional morphology. This volume is really indispensable for anyone wishing to keep up with the latest developments. For information about the 2009 Symposium, see www.ams.jrc.it/mdigest.

In my last survey, I mentioned a book by R.M. Haralick on *Mathematical Morphology*, to be published by OUP. This has still not materialised, even though it has a price and even an ISBN.

3. Electron microscopy and holography

Thus, as in other areas of materials science, the structure–property relationship is the key to understanding chocolate. Tempering, composition control, and even the seeding of the chocolate with different chocolate crystals all play an important role in chocolate making. The complication from a materials science point of view is that the final desired property is ultimately senso-aesthetic: a combination of taste, smell, texture, color, and form.

A recent poll of the community by The Minerals, Metals, and Materials Society (TMS) has identified the top 100 materials science moments. Sadly, chocolate was nowhere to be found on the list. This is shame, because chocolate is no less remarkable and technically sophisticated a material than semiconductors or steels. Through our ingenuity, we have found a way to create a cold, dark, brittle piece of refined tropical rain forest nut designed for one purpose only—to put it in your mouth and wait while it melts and floods your senses with warm fragrant bitter sweet flavors and simultaneously ignites the pleasure centers of the brain. Despite our scientific understanding, words or formulas are not enough to describe this sensual material. It is a material poem, as complex and beautiful as a Shakespearian sonnet. If materials science has no place for materials poetry such as this, then it is pity indeed. We are poorer as a community without the Lady of the Flake.[1]

Mark Miodownik, *Materials Today*, 10(4), 2007, 6

Pride of place goes to the Italian Society of Microscopical Sciences (SISM), which has assembled a 362-page book on the history of microscopy in Italy from 1956, the year in which the Italian Society of Electron Microscopy (SIME) was founded, to 2006, its fiftieth birthday [5]. It opens with a brief history of the SIME by U. Valdrè, who does not limit himself to the 50-year interval but reminds us of the Siemens microscope installed in the Istituto Superiore di Sanità in Rome in 1942, heavily used until the German troops repatriated it in 1943. G.S. Trabacchi then had a home-made microscope built in the ISS, "utilizzando i disegni rilevati dallo strumento Siemens la notte prima del prelievo"! He was the founder-president of the SIME and on his death in 1959, he was succeeded by D. Steve Bocciarelli (whom some older ultramicroscopists will remember fondly from the Rome EUREM in 1968). I cannot list all the 24 other contributions but there is much of the highest interest: SEM, by the late P.G. Merli and V. Morandi; HREM by A. Parisini; an introduction to electron holography by G. Pozzi; Remote electron microscopy by M. Vittori Antisari and S. Migliori; FIB, confocal microscopy, scanning probe microscopy, all are present. The second half of the book contains chapters on applications in the life sciences, notably cell biology but also plant pathology (R. Musetti). To conclude, G. Bottiroli and A. Gallone give an account of 'I beni artistici: un patrimonio da salva … guardare al microscopio' and show the remarkable quality of the Italian contribution to this subject. The book is beautifully produced with some colour, though the quality of the half-tones struck me as uneven.

The *Annual Review of Materials Research* often contains individual essays of interest to ultramicroscopists and volume 37 [6] is particularly rich in such papers. Thus, W. Wulfhekel and J. Kirschner describe "Spin-polarized STM of magnetic structures," D.N. Seidman comments on "Advances and applications [of] three-dimensional atom-probe tomography" and D.J.H. Cockayne studies "nanovolumes of amorphous materials using electron scattering." There are two contributions on electron holography, still rather an outsider despite the remarkable work of the Dresden, Hitachi and Tempe groups. H. Lichte et al. give a real tutorial (50 pages) on the application of electron holography to materials questions, largely confined to their own work (Tonomura is cited only once, his book of 1994). M.R. McCartney and D.J. Smith also contribute a long chapter on "Electron holography: phase imaging with nanometer resolution," again showing vividly how much this technique has to offer the microscopist, The 128 references reflect the range of specimens that have been studied by this means though here again, the Japanese contribution is under-represented.

Books on electron microscope techniques are doubtless being published "in the vernacular" but those not in English rarely come my way. It is therefore all the more agreeable to draw attention to a two-volume guide to specimen preparation for TEM by J. Ayache, L. Beaunier, J. Boumendil, G. Ehret and D. Laub [7]. Volume I, *Méthodologie*, in fact contains more than the title suggests, for chapters on types of specimens (materials and biological sciences) and on microscope imaging modes (SEM and STEM as well as TEM) precede those on specimen preparation itself. Volume II, *Techniques*, takes the reader systematically through the various ways of preparing specimens for observation in the TEM. The books are attractively printed, with abundant illustrations printed on glossy paper and French-speaking microscopists should think themselves very fortunate to have such a guide at their disposal. Jeanne Ayache, the leading author and begetter, opens each volume with one of her pensées: "Le cadeau de la microscopie, c'est, au delà de la beauté des images, de nous donner accès à l'Art de la matière et de nous emmener au cœur des mécanismes, 'de la structure de la matière inerte à la complexité du vivant: là où l'infiniment petit et l'infiniment grand sont reliés … Une leçon de vie et d'humilité'" for *Methodologie*.

Electron Microscopy, Methods and Protocols, edited by J. Kuo, is intended for life scientists [8]. This is a thoroughly revised edition of a book published in 1999 and covers TEM, SEM and mass spectrometry. The material is organised according to the microscopist's needs; thus, a part of the group of TEM chapters is "for the benefit of those who only require routine TEM images through ultramicrotomy, sectioning and then positive staining. Separate chapters are destined for those using high-pressure freezing and cryoultramicrotomy; another group covers negative staining and immunogold labelling and related matters; a last cluster covers TEM crystallography and cryo-TEM tomography, and there is a chapter on EELS. In the SEM section, environmental SEM and cryoscanning are now included and the book ends with a general chapter on SIMS for biological and biomedical research and another on SIMS and MIMS in the study of higher plants; here the copy-editor has clearly dropped off after reading more than 500 pages, with the result that we are told that "Practical considerations … are essential to avoid miss-interpretation of some SIMS results," enough to make feminist microscopists burn the book, especially as the author of the chapter is *une* microscopiste. Forty-nine authors have written the 28 chapters but the recipe format renders the material reasonably homogeneous.

It is reassuring to see that publishers continue to produce highly specialised microscopy texts, even though the potential audience cannot be very large. A recent example is *Application of Cathodoluminescence Imaging to the Study of Sedimentary Rocks* by S. Boggs and D. Krinsley [9], the seven chapters of which will be appreciated by the geological community. Two chapters tell us what cathodoluminescence is and describe the relevant instruments. The remainder of the book explores many applications: Provenance interpretation, Diagenetic minerals and fabrics in siliciclastic sedimentary rocks, Luminescent characteristics and diagenesis of carbonate sedimentary rocks and Miscellaneous applications of cathodoluminescence to sedimentary rocks.

[1] The Lady of the Flake is a Cadbury's TV advert. It can still be viewed on www.youtube.com. Search bath Cadbury.

Among the latter are archaeological applications; "Perhaps the most interesting potential archaeological application of CL from a sedimentological point of view is the use of CL to trace so-called *temper* in pottery. Temper is sand grains, crushed rock or ground-up potshards [sic] that are added to clay to reduce shrinkage and cracking during drying. Sand grains can be effectively characterized by CL, which may allow the grains to be traced to their geologic sources…. In a different approach to the same problem, Gordon Goles [a colleague of the authors'] initiated a study of quartz grains in potshards from Fiji by using the same method for provenance analysis as that described by Seyedolai et al. This method is based upon study of CL fabrics in quartz rather than CL color…. Basically, volcanic quartz primarily displays zoned CL patterns, plutonic quartz is characterized especially by spider-like fabrics (dark streaks and patches), and metamorphic quartz displays homogeneous or mottled CL. Goles reported that he had made progress in his investigation; preliminary results, on the basis of CL fabric study, indicated that the temper grains in Fiji pottery could be linked to nearby sand dunes. Unfortunately, Gordon died before his work was finished and the results were never published. Nonetheless, this technique for studying temper grains clearly has potential. A possible problem with the technique, as well as the use of CL color in ceramic provenance, has to do with the temperature used in firing pottery. Is it high enough to affect CL emissions in quartz? Cathodoluminescence experiments on fired German quartz sands apparently show that there are no CL changes with temperature; however, this potential problem may need further research." Highly specialised, therefore, but no doubt essential if you are a sedimentologist.

For many years, *Transmission Electron Microscopy* by the late Ludwig Reimer was arguably the best general book on the subject but I have to admit that that it has been partially unseated by *Transmission Electron Microscopy and Diffractometry of Materials* by B. Fultz and J. Howe, now in its third edition [10], though there are areas for which Reimer is still better; the coverage of electron optics, in particular, remains very superficial in Fultz and Howe. The earlier editions have been mentioned here and I therefore concentrate on the novel features of this new edition. The authors tell us that "There are significant changes in" the chapters on Diffraction and X-ray powder diffractometry, Scattering diffraction contrast in TEM images, Diffraction lineshapes and Patterson functions and diffuse scattering. Chapter 11, "High-resolution STEM imaging" is new and the title is a little misleading for it is here that "Lens aberrations and their correction" are described, for both the fixed-beam and scanning transmission electron microscopes. Newcomers to this title may like to be reassured that, despite its formidable 754 pages, this is essentially an introductory text. Thus, "Multi-beam dynamical theories of electron diffraction" (the last section of the book) occupies less than three pages, only enough to give the flavour of the subject. It is a book that enables you to get the hang of a very wide range of topics, a great merit, but in some cases you will need to look elsewhere to go deeply into them—it could probably not be otherwise!

H. Liebl has just published *Applied Charged Particle Optics* [11], in which the emphasis is on electrostatic lenses and condensers and magnetic sector fields with a chapter on applications. This is a short book (128 text pages) and follows the course notes of Liebl's lectures; it is "intended to help physicists who have to design their own apparatus or to help them to better understand instruments they have to work with." The five chapters cover Basic optics of lenses, Electrostatic deflection, Magnetic deflection, Image aberrations and Fringe field confinement. The treatment is very elementary but this should not be regarded as a shortcoming, merely as an indication that the student who wishes to go more deeply into the subject will need to find a more advanced text. From Liebl, he will learn the basics of focusing and (large-angle) reflection, the acceleration of particles from plane surfaces, the action of electrostatic condensers and magnetic sectors, both uniform and non-uniform, and the aberrations of lenses and deflectors. There are numerous clear diagrams and the book succeeds in its modest aim: to get beginners started in a fairly painless fashion. The references are for the most part ancient. Some guidance to "Further reading" would have been welcome—the most recent general books cited are Zworykin et al. (1945) and Harting and Read (1960), both excellent in their way but hardly "cutting-edge." Even Wollnik's book in not mentioned.

Mainly for the higher current-density community, there is a new edition of M. Reiser's *Theory and Design of Charged Particle Beams* [12]; Wiley-VCH tell us that "This revised and updated monograph offers a broad synoptic description of beams in accelerators and other devices with negligible to strong space charge effects. The book develops material in a systematic way and discusses the underlying physics and validity of theoretical relationships, design formulas and scaling laws …. [It] has significant additional content, which covers experiments, theory, and simulation in beam physics research since 1993." In fact, the main text (six chapters) is virtually unaltered from the first edition, only misprints and other trivial errors being corrected. This begins with an introduction in which the history of the subject is summarised and the various types of sources are discussed. Then comes a "Review of charged particle dynamics," which I found very clear with much helpful explanation. A third chapter covers "Beam optics and focusing systems without space charge," with an account of magnetic and electrostatic lenses and other optical elements. This too is clear, though there is more reliance on thin-lens theory and hard-edged models (for quadrupoles and sector magnets) than the electron microscope designer can allow himself. Chapters 4–6 are largely for accelerator physicists: "Linear beam optics and space charge," "Self-consistent theory of beams" and "Emittance growth." In this last, the description of the effect of spherical aberration on the trace-space ellipse is of wide importance and the approach to the Boersch effect too is of general interest. There is then a long new chapter, covering developments in the subject since 1993, with particular emphasis on the work at the University of Maryland where Reiser is based. I have no doubt that this will be found extremely valuable by the accelerator community for whom it is written. Wiley-VCH can be congratulated on the quality of the production; the book is nicely printed and bound and still manageable despite its 650-odd pages.

Scattering has a vast literature but with ever-increasing computing power, the older collections of data are being updated and extended. *An Introduction to the Passage of Energetic Particles through Matter* by N.J. Carron [13] is a promising source book for "Knowing where to access [cross-section data], extracting a needed subset from all that is available, knowing how to interpret the format in which it is presented, can be time-consuming tasks …. It seemed worthwhile to collect in one place as much [*sic*] of these often needed data as possible, together with enough background physics so the reader can feel comfortable applying them, having some understanding of where they come from and why they have the order of magnitude they have. The idea is to make up-to-date data available and understandable to non-specialists. The book and its accompanying data CD and contour plots are intended to be a working reference for scientists and engineers in industry, educational institutions, and laboratories, providing ready access to useful data. We have also tried to digest the data in the form of useful graphs, showing dependencies over a wide range of the independent variable(s), allowing quick approximations of a quantity. And it was decided to include much

of the numerical data on a CD-ROM included with the book." These seem excellent reasons for a book such as this, which has chapters on photons, electrons, protons and heavier ions and on "Selected topics on neutron interactions." However, I am not sure how successful it is for the electron microscopist—very few of the references to Chapter 5 of Reimer's *Transmission Electron Microscopy* appear in the list at the end of Carron's chapter on electrons.

I have mentioned Formatex in these columns, notably in connection with their Microscopy Series, to which microscopists were invited to contribute (and pay for the "privilege"). Two volumes on *Science, Technology and Education of Microscopy, an Overview* [14] appeared some years ago, but despite innumerable promises, review copies were never sent to me. Recently, I was told that I could have review copies of the above title and of its successor, *Current Issues on Multidisciplinary Microscopy Research and Education* [15] if I was willing to pay for the postage—this I did and I can now report on the contents. The two volumes of the "Overview" appeared in 2003 and their 858 pages include 100 short contributions. These have the rather arbitrary character of papers in a large congress: the section on biology, for example, ranges from "Scanning electron microscopy in paleoanthropological research" (A. Romero and J. de Juan) to "SEM analysis of the cellular bio-hospitality and roughness of glass dental ceramics" (T. Traini et al.). The more recent volume, *Current Issues …* (2005), continues in the same vein, 34 papers on such topics as "The effect of abrasives in the diet" (A. Romero and J. de Juan again), "Basic principles of molecular recognition force microscopy" (P. Hinterdorfer), "Assembly and accumulation sites of maize mosaic virus (Rhabdoviridae) in plant host and insect vector using transmission electron and confocal laser scanning microscopy" (E.-D. Ammar et al.), "butterfly wings" (Zs. Bálint et al.), "aquatic biofilms" (J. Morató et al.), "unculturable bacteria" (A. Ciancio et al.) and numerous papers on AFM and other techniques. I was not aware that some bacteria resist the biologists' efforts to study them but A. Ciancio et al. confirm that many bacteria are "fastidious or unculturable"—indeed, "The microbial diversity studied and described thus far on artificial media represents only a minor fraction of the total number of species present on earth." AFM seemed a good way of studying these elusive germs, and A. Ciancio et al. show what can be achieved.

The 2007 congresses do not of course include an international microscopy congress or any of the regional congresses in Europe or Asia; conversely, major meetings were held in the USA (the annual MSA congress, in Fort Lauderdale), in Prague (the eighth Multinational Congress on Microscopy, formerly MCEM), in Saarbrücken (the DGE meeting), in Glasgow (EMAG 2007) and in Peru (CIASEM). I have not seen proceedings of any other national meetings apart from that of the Irish society, now printed in the Royal Microscopical Society's *In Focus* (formerly *Proc. RMS*).

Microscopy and Microanalysis 2007 [16], the MSA meeting, is as usual recorded in a supplement to the MSA journal of the same name. Of the 1739 pages of abstracts, only 210 appear in print, the remainder relegated to the CD-ROM (or to the *M&M* website). May I yet again suggest to publishers and organisers that this drastic reduction of the number of printed papers is excessive. While I do not regret the cumbersome volumes that used to include *all* the abstracts, I do think that a book of, say, 500 pages with only one tightly printed page per abstract would be more useful and still perfectly manageable. The contents as usual cover the whole spectrum: medicine, biology (animals and plants and microbes), materials science and instrumentation. In this last area are extremely interesting papers on the latest developments in aberration correction and in holography and a large section on EELS and energy-filtered imaging. There is also a single paper on electron tomography for materials science by our editor (CD-ROM only) and a section of "New phase contrast methods for TEM" with papers on phase plates. H. Rose makes it clear that microscopes will need phase plates as well as aberration correctors for optimum performance. The 36 aberration–correction papers form two groups, one largely instrumentation, the other largely applications. In the former, the progress reports of A.R. Lupini and S. Pennycook (STEM), P. Hartel et al. (an advanced hexapole C_s–corrector, U. Dahmen (TEAM), M. Haider et al. (a C_s–C_c corrector for TEAM) and M. Matijevic (monochromator) give a good snapshot of the situation. These corrected instruments are now yielding new results: funding agencies please note!

The German Microscopy Society met in Saarbrücken in September 2007 and another supplement to *Microscopy and Microanalysis* [17] contains *all* the abstracts (460 pages). The three parts cover Instrumentation and Methods, Applications in Life Science and Applications in Materials Science. The book opens with the session on Progress in instrumentation and electron optics, which itself opens with an account of the latest program suite for electron optical calculations by B. Lencová and J. Zlámal. This is fast, versatile and powerful, being able to calculate not just the properties of lenses but also of deflectors and multipoles and even detectors. P. Hartel et al. then describe their first results with an advanced hexapole corrector, capable of eliminating third and fifth order spherical aberration and many of the parasitic aberrations. The paper by S. Irsen et al. describes the performance of a related instrument, an HR(S)TEM with both an electrostatic monochromator and a hexapole C_s-corrector. The next two papers take up the question of phase plates and R.R. Schröder et al. describe a type of anamorphotic phase plate. There are also papers on FIB optics (M. Rauscher et al.), on the SESAM microscope (E. Essers et al.) and on nanorobots for SEM and SIM (S. van Offern and V. Klocke). These are followed by long sections on Progress in atomic resolution imaging methods, Analytical (S)TEM and spectroscopy, Advances in SEM, LEEM and SPM, Specimen preparation, Tomography and cryo-techniques. Quantitative diffraction techniques and Miscellaneous. The equally long parts on applications are likewise of the highest interest and the DGE can be proud of such an impressive collection.

In 2006, a meeting on "Materials Research in an Aberration-free Environment" was held just before the MSA congress and a regular issue of *Microscopy & Microanalysis* [18] records eleven of the papers delivered there. There are contributions from many of the laboratories equipped with corrected instruments; I found the article by D. Geiger et al. on "Electron holography with a C_s-corrected TEM" especially useful.

Since 1993, six national (electron) microscopy societies have been organising biennial "Multinational" congresses, the latest of which was held in Prague in June 2007. This too is a very impressive collection [19], 558 pages of (mostly 2-page) abstracts beginning with the three plenary lectures: O. Křivánek et al. on Atomic resolution nanoanalysis, where the emphasis is on techniques rather than on instrumentation; A. Howie on Extrapolating from 50 years of dislocation imaging—reaching into the core; and R. Lim et al. on "The use of microscopes: from the bench to the patient." Instrumentation again begins with a paper on "CAD in electron optics" by B. Lencová, which unfortunately has no illustrations but nor does Rose's presentation of "Optimum imaging modes in electron microscopy," which follows it: "Our considerations show that the correction of chromatic and spherical aberration is mandatory to achieve optimum conditions for the imaging of biological and solid objects. In addition a micro-phase plate is necessary which shifts the phase of the non-scattered waves by $\pi/2$." The section continues with papers by V. Krzyzanek and R. Reichelt on "Quantitative high-resolution SEM

in the transmission mode: a new microanalytical tool"; I. Müllerová et al. on "Parallel acquisition of the angular distribution of BSE in SEM"; and "A new set of software tools for holographic reconstruction and analysis with fast automatic phase unwrapping" by L. Ortolani et al. For the remainder, let me just list the sections: High resolution and analytical TEM, SEM and microanalysis, Advances in LM methods, Specimen preparation methods in materials science, FIB, Ceramics, composites and minerals, Nanostructures, nanoparticles and catalysts, Nanostructural materials and interfaces, Metals and alloys, Polymers, Imaging of molecules, cells and tissue in vivo, Image analysis and stereology in microscopy, Ultrastructural cryomicroscopy, tomography and EFTEM in biology, Advanced methods of biological sample preparation, functional organisation of microorganisms, cells and tissues, and finally, Microscopy in human health. Somewhat to my astonishment, this last section includes a paper on mouse brains! There are also a great many posters, not classified by subject.

A congress that is not well known outside South America is the CIASEM congress, the ninth of which was held in Peru in September 2007. The Proceedings [20] were produced on CD-ROM and can be read free on the congress website (www.ciasem2007.com). The papers are classified into the familiar groups: Plenary lectures, Instrumentation, Materials Science and Biomedical Science. Among the plenary lectures is a most interesting comparison of microscopy using helium ions and low-voltage field-emission SEM by B.J. Griffin. Instrumentation begins with an account of 30 years of X-ray analysis in TEM by D.B. Williams and M. Watanabe; H. Lichte surveys electron holography after which several papers discuss C_s-corrected microscopy. HREM tomography is covered by H.A. Calderón et al. and in the same area, L.S. Gómez et al. examine HRSTEM and nanotomography in rare earth oxide nanoparticles for luminescent applications. A. Eades lists problems and progress in EBSD. The session concludes with a paper by R. Fandrich and G. Ocharan (the congress organiser) on SEM-based quantitative mineralogy. I should have liked to quote from some of the submitted papers, especially those in which South American specimens appear, but most of these are in Spanish. Sufficient to say that there is plenty of interesting new material here. For information about the 2009 CIASEM Congress, to be held in Argentina, watch their site www.ciasem.com. (Note: .com has now replaced .org.)

There is no news of the Proceedings of EMAG 2007 at the time of writing (April 2008) but it will doubtless have appeared on-line in the *J. Phys. Conf.* series (open access) by the time you read this.

The proceedings of the 31st annual symposium of the Microscopy Society of Ireland are bound into *In Focus* [21], not just a loose insert that got lost in library collections as in the past. S. Nakahara opens the collection with a Historical Perspective of Image Simulation in TEM. "We have taken various stages of painful steps in reaching the present computer-aided age" writes Nakahara feelingly and many of those who are not absolute beginners will agree fervently. "This presentation will describe how computers were used for image analysis and provide some historical background based on the author's experience." The penultimate abstract caught my eye as it deals with a very contentious subject, the hydrogenation of vegetable oil, against which the popular health magazines are currently warning us. "During the hydrogenation process, the double bonds of the fatty acid chains are saturated while a certain amount of the remaining bonds are isomerised by *cis*/*trans* conversion and positional shift in the fatty acid chain. Saturates have long been known to be detrimental to peoples [*sic*] health and in recent years there has been increasing concern that trans fatty acids increase the risk of coronary heart diseases. For this reason, there has been a lot of interest in reducing the level of trans fatty acids in hydrogenated oils. Currently, the catalyst used in industrial hydrogenation is a nickel catalyst operated under high temperatures and pressures. The objective of this study was to evaluate the dependence of catalytic activity and *cis*/*trans* selectivity on the support features and various noble metals. The work involved the synthesis of various Pd and Pt catalysts supported on a range of different supports. Al_2O_3, ZrO_2, TiO_2 and SiO_2. Sunflower oil was then hydrogenated in a batch reactor using these catalysts under a variety of conditions. The changes in the iodine value, fatty acid composition and trans fatty content during the hydrogenation were investigated on the samples taken at 1 h intervals." The abstract tantalisingly stops there. What did S. McArdle et al. conclude? Have they stopped eating industrial biscuits? Perhaps the answer will be given at the next MSI meeting.

The same issue of *In Focus* contains a beautifully illustrated article by B.J. Ford, written to mark the 375th anniversary of Leeuwenhoek's birth. The comparison of the work of Hooke and Leeuwenhoek is strongly recommended, upsetting as it does some widely held beliefs (and doubtless some Dutch historians of microscopy): "Scholars often talk of these simple [diminutive, crude, single-lensed] microscopes as a 'Leeuwenhoek design'. This can be faulted too, for the design was actually one of Hooke's. The description is hidden within the Preface to Micrographia …. On the 22nd page of the Preface may be found Hooke's own design for a home-made microscope. The description was the inspiration for Leeuwenhoek. 'Take a very clear piece of a broken Venice glass, and in a Lamp draw it out into very small hairs or threads…' he wrote. And then, melt them 'into a small round globule … rub them until they become smooth' before mounting the tiny lenses in a needle hole in 'a thin plate of Brass …' and what is the result? A typical 'Leeuwenhoek' microscope. It was, in reality, a Hooke microscope." Ford then goes on to show that many of the images shown by Hooke were in fact obtained with such a single-lens instrument and not with his compound microscope.

Micro- and Nanoengineering 2006 is recorded in *Microelectronic Engineering* [22]. These are, as usual, real proceedings, not just abstracts, with the result that the book has 1156 pages (plus front matter)! Faced with 16 pages of Contents, I am at a loss to know what to mention here, though I strongly approve of printing full proceedings and leaving posterity to decide what is worth reviving and what can be allowed to sink into obscurity. "The role of MEMS in maskless lithography" seems a good springboard, as it is by a former editor of *Ultramicroscopy*; P. Kruit "dreams about writing the pattern directly into the resist on a Si wafer, without the intermediate step of mask production …. The challenges, however, are enormous …. The conclusion will be that only massively parallel writing is an option, whichever concept we choose. This parallelism can only be achieved if the system components are miniaturised to micron sizes. This in turn is only possible with micro-electro-mechanical systems (MEMS) technology." That is in a section on Mask-less Technology, whereas it is the section on Electron and Ion Beam Lithography that is usually closer to ultramicroscopy. The latter is opened by P. Hahmann et al. on "High resolution variable-shaped beam direct write," followed by J. Gierak et al. on "Sub-5 nm FIB direct patterning of nanodevices." R. Aldana and F. Pease have devised an ingenious travelling-wave deflector capable of deflecting many parallel beams. The other 11 sections cover the topics traditionally included in MNE. As always, this volume and its sisters or rivals, which record the American three-beams meeting (EIPBN) and the Japanese Microprocessors and Nanotechnology congress, are essential reading for nanoengineers.

4. Electrons, pro and con

Tesman: Have you heard anything of Ejlert? Since I went away, I mean?

Miss Tesman: No, only that he's supposed to have brought out a new book.

Tesman: What? Ejlert Lövborg? Just recently? Eh?

Miss Tesman: Yes, so they say. I shouldn't think there can be much in it, would you? Now when your new book comes out, that will be quite another story, Jörgen. What is it going to be about?

Tesman: It's going to be about domestic crafts in Brabant in the Middle Ages.

Miss Tesman: Well, well! To think you can write about a thing like that!

Henrik Ibsen, Hedda Gabler

Representing Electrons by T. Arabatzis has the subtitle *A biographical approach to theoretical entities* [23]. After chapters intended for his fellow historians and philosophers of science, Arabatzis challenges our preconceptions with a chapter on Rethinking "the discovery of the electron," of which Section 1 is entitled "What is wrong with the received view?". The latter asserts that "J.J. Thomson discovered the electron in 1897, while he was experimenting on cathode rays at the Cavendish Laboratory" and, with a few qualifying phrases, most of us would agree with this, though friends and descendents of Wiechert would presumably demur. But "the received view is problematic, on both historiographical and philosophical grounds. On the historiographical side, it downplays several British and Continental developments that were quite decisive for the gradual acceptance of the electron as a universal, subatomic constituent of matter. On the philosophical side, it presupposes a realist perspective toward unobservable entities and requires a theory of scientific discovery that would support such a perspective. As far as I can tell, no such adequate theory has been developed (see below)."

Our preconceptions badly shaken, we are ready to face "The Birth and Infancy of the Representation of the Electron," which does little to prop them up. The official midwife was George Johnstone Stoney, a very colourful Irishman who devised a new simplified musical notation, ostensibly less difficult than the standard one, studied "the experiment of Mahomet's coffin" and "the energy expended in propelling a bicycle" (an Xtraordinary, which Stoney and his son tested "on a wet gravelled pathway in Palmerston-park, Dublin, up a trifling incline of 1 in 160, with the wind") and who gave the electron its name, indirectly at least, for he intended the word as a unit, not a particle. But the idea of small charged particles was broached much earlier. Arabatzis quotes from a host of ur-Thomsons, such as Richard Laming who conjectured "the existence of sub-atomic unit-charged particles and pictured the atom as made up of a material core surrounded by an 'electrosphere' of concentric shells of electrical particles" in the 1840s, a very bright conjecture indeed! Weber, Faraday, Helmholtz, Zeeman, Larmor, Lorentz and Wiechert are all involved in the run-up to J.J. Thomson's papers of 1897. All their ideas are sifted and assessed and so muddy are the waters stirred up by Arabatzis that he is forced to conclude that we need to re-think the very notion of "discovery." There are five more chapters: The genesis of the quantum electron, Between relativity and correspondence, "How the electrons spend their leisure time": the chemists' perspective, Forced to spin by Uhlenbeck and Goudsmit and, to conclude, Identifying the electron: meaning variance and the historicity of scientific realism. I cannot do better than quote the last words of the book: "However, all these elements of continuity do not sufficiently establish the electron's existence." I hope that funding bodies who are being asked for vast sums of money for aberration correctors do not read these words.

5. History

Mephistophilis [to Faustus]: Hold, take this book, peruse it thoroughly:
The iterating of these lines brings gold.
Christopher Marlowe, *Dr. Faustus*

The great names of early 20th century physics may be well known but the stories behind the names have not always been told. I make no apology for drawing attention to P. Rife's *Lise Meitner and the Dawn of the Nuclear Age* [24], which brings to life numerous figures of the time—Otto Hahn, Otto Stern and many others, including Otto Frisch, Lise Meitner's nephew, whose lectures on nuclear physics in my undergraduate days were enlivened by reminiscences of his experimental work, perturbed by the ash from Stern's cigar that fell into his apparatus. I could fill many pages with moving and deservedly memorable quotations but must limit myself to a few, beginning with the last sentence of the Epilogue: "The humble gravestone Frisch erected for her in Cambridge, with the equation for nuclear fission carved in stone, captures the spirit of this remarkable person. Her epitaph simply reads, 'A physicist who never lost her humanity'. But it was not her love of humanity or world peace that cast a shadow over her major scientific achievements. Prejudice, exclusion, and even denial of her major role in scientific discoveries were themes throughout her eighty-nine years—grim reminders of the social and political nature of science, the political realities of the Nobel Prize selection process, and the very clear ties that politics, funding, and choices of technological applications have to the worldwide scientific enterprise itself. When the atomic bomb exploded, the nuclear age was ushered in. Lise Meitner was a pioneer from the very dawn of this nuclear age." Lise Meitner was born in 1878 in Vienna, grand-daughter of a "beautiful widow from Moravia," who "sang to keep up the family spirits … when their family house burned down and cholera broke out in their village." She did "not fit into the model of a 'proper' Viennese young lady," who was expected to be "silly and untaught, well-educated and ignorant, curious and shy" (Stefan Zweig). She was one of only four girls to pass the entry examination to the University of Vienna and "in the autumn of 1901, many male faculty members and students may have been astonished to see a young *fräulein* enter the University of Vienna's crowded lecture hall, as astonished as Lise was when she was given the opportunity to see 'real' physics apparatus and an experimental lab!" Later, she was appointed 'Scientific Associate' at the Kaiser-Wilhelm-Institut in Berlin, opened in 1912 by the Kaiser himself, to whom she was presented: "It is easy to picture four-foot ten-inch Lise Meitner's shy response to the Kaiser's 'friendly remarks' when she was formally introduced as a well-known woman scientist and 'Institute Guest Physicist'. She was not political. Far from her Austrian home, meeting the Kaiser was an honour that made a lifelong impression." Then came the first world war, the 1920s and the horrors of the 1930s and WWII. P. Rife takes us almost day by day through the wartime years and makes clear Lise Meitner's fundamental contributions to nuclear physics. The failure of the Nobel committee to award the prize jointly to her, Frisch, Strassmann and Hahn but to Hahn alone is analysed at length and we should not forget that "Otto Hahn gave part of the large financial award that accompanied the Nobel Prize to Lise Meitner. Characteristicaly, she immediately decided to pass it on in a large contribution to the Emergency Committee of Atomic Scientists …. The Committee, chaired by Albert Einstein, consisted of scientists who were greatly concerned about the politicization

of atomic research. Einstein promptly sent Lise a friendly acknowledgment."

Much closer to ultramicroscopy are the articles by S.F. Johnston on the history of holography. The first of these that I have seen is on the activities of George Stroke in holography [25]; Stroke's name appears on several papers on electron holography, in particular, on light-optical reconstruction of electron micrographs, of the 1970s. His book on holography is still in use, despite Emil Wolf's devastating review in *J. Opt. Soc. Amer.* 57 (1967) 405–406. Johnston's essay is extremely revealing about the scientific politics of early holography—he has had access to much archival material—but I do not think that he can have met Stroke in person. Back in the 1970s, Stroke came to Cambridge and offered to give a colloquium at the MRC Laboratory of Molecular Biology; Aaron Klug asked me if it could be held in the Cavendish Laboratory instead (where we held regular afternoon colloquia) and this was indeed arranged (17 December 1971). I mention all this because Stroke's courtesy and charm is an important element in the story, though some found him fulsome; I still have the warmly appreciative bread-and-butter letter that he sent afterwards. Some of Stroke's success with Gabor and others was surely due to these personal qualities. I do not suppose that Stroke will write an appreciative letter if he reads Johnston's indictment, well-buttressed with documentary evidence.

The other paper by S.F. Johnston describes the difficult first years of holography, from the early thinking that led to Gabor's *Nature* paper of 1948 to the end of the 1950s [26]. His account is very nicely written and has the merit of quoting numerous letters from those involved, often from the Gabor archive at Imperial College. These bring to life many of the personalities, not just those known to electron microscopists such as M.E. Haine, J. Dyson and T. Mulvey but also G.L. Rogers, Sir Lawrence Bragg, P. Kirkpatrick, H.M. El-Sum, A.V. Baez and A. Lohmann. The exchange of correspondence between Haine at AEI and Gabor at Imperial College is particularly interesting and outspoken but by the end of the 1950s, "Allibone dismissed the work as one of the many white elephants that the company had produced: 'We spent a great amount of time investigating this idea, solving very many different problems in sequence, such as keeping the specimen free from contamination for half an hour and free from vibration to the order of 1 Å and holding the voltage constant to 0.1 V in 100 000 V for half an hour, but the best holograms we could produce failed to give us a reconstructed image as good as the image we could then achieve by direct microscopy and we were obliged to drop the work. To that extent, therefore, it can be regarded as having been unsuccessful, but out of it we have learned so much about microscopy that the E.M. 6 has been produced capable of a resolution of 5 Å'."

6. Other topics

> *I should hardly have called myself by the hideous title of "Professor" [A title associated with 'thaumaturgists and prestidigitators'].*
> Matthew Arnold

J.C. Russ's *Image Processing Handbook* has gone into a fifth edition [27], in which "more than 600 new and revised figures [have been] introduced … and the reference list has been expanded by more than 20% …. The reader will find expanded discussions on deconvolution, extended-dynamic-range images, and multichannel imaging, the latter including new material on principal-components analysis. The sections on the ever-advancing hardware for image capture and printing have been expanded and information added on the newest technologies. Russ reminds us that his book does not include the theory on which the image processing techniques are based—we can hardly describe this as a weakness of a book that is already 800 pages long but the user of the book must imperatively have one or two of the standard texts on image processing beside it. The publishers have produced a very handsome volume, with colour throughout.

Next, two volumes on image processing in which the mathematics *is* included: *Geometric Partial Differential* Equations and *Image Analysis* by G. Sapiro [28] and *Analytic Tomography* by A. Markoe [29]. The titles of the eight chapters of Sapiro's book give a good (if somewhat forbidding) idea of the level: Basic mathematical background (69) pages; Geometrical curve and surface evolution (with a section on continuous mathematical morphology); Geodesic curves and minimal surfaces; Geometric diffusion of scalar images; Geometric diffusion of vector-valued images (including vectorial median filters and color self-snakes); Diffusion on non-flat manifolds; Contrast enhancement; and Additional theories and applications. It is worth pausing to consider these, which bring the theory right down to earth. Sapiro has a section on "Image repair: inpainting", which describes how scratched films, damaged photographs and "vandalized images" can be repaired. Fig. 1 is a convincing example of the power of the methods.

Markoe's text on tomography [29] attempts to please more than one audience, from the user of a CT scanner to the applied mathematician concerned with the principles. The latter may indeed enjoy reading the introductory material but I doubt whether the former will get very far. Even Chapter 1, which "has almost no mathematics in it," expects the reader to take

$$R_0 f(s) = R_{\pi/4} f(\tfrac{1}{2}) = 2\sqrt{2} - 1$$

in his stride. Technical Note 1 begins with the words "For those readers who know some calculus …" but for the rest of the book, they are expected to know a great deal more than "some calculus," hardly surprising for a volume of the *Encyclopedia of Mathematics and its Applications*. Subsequent chapters cover "The Radon transform", "The k-plane transform, the Radon-John transform", "Range and differential equations" and "Generalizations and variants of the Radon transform". A great deal of information is gathered here but it must be said that it is not easy to retrieve.

G.T. Herman and A. Kuba have produced a successor to their *Discrete Tomography* of 1999; the new collection, *Advances in Discrete Tomography and its Applications* [30], begins with the editors' introduction, 16 pages long, which is in fact a guide to publications that have appeared since 1999, with the result that there are only five pages of text, the 191 references filling the remainder. The contributions are classified as "Foundations of discrete tomography", "Discrete tomography reconstruction algorithms" and "Applications of discrete tomography". The first part, Foundations, begins with a useful introduction to discrete point X-rays by P. Dulio et al. and is followed by five mathematical articles. It is Part III, Applications, that is of most interest here; H.Y. Liao and G.T. Herman analyse "Direct image reconstruction–segmentation, as motivated by electron microscopy": "Our aim is to produce a tesselation of space into small voxels and, based on only a few tomographic projections of an object, assign to each voxel a label that indicates one of the components of interest constituting the object." Later contributions discuss grain maps of polycrystals (A. Alpers et al.), nondestructive testing (J. Baumann et al.), emission discrete tomography (E. Barcucci et al.) and computerized tomography (Y. Gerard and F. Feschet).

My next title, *Exploratory Data Analysis using Fisher Information* [31] comes from an author who has often appeared here: together with R.A. Gatenby, B.R. Frieden has edited a collection of articles inspired by his earlier work on Fisher information, and of the nine chapters, Frieden is author or co-author of six.

Fig. 1. Restoration of a (colour) image and removal of superimposed text (from Sapiro: *Geometric Partial Differential* Equations and *Image Analysis*, courtesy of the author and Cambridge University Press).

Here, the applications go far beyond physics, which has been Frieden's main target hitherto. Chapter 1 is an introduction to Fisher information by Frieden, after which he, R.J. Hawkins and J.L. d'Anna apply it to financial economics. Gatenby and Frieden then consider 'Growth characteristics of organisms', with carcinogenesis as the prime example, Chapter 4, by A. and A.P. Plastino, is a really fascinating account of 'Information and thermal physics', and in particular of 'Fisher thermodynamics'. "We now show", say the Plastinos, "that FIM [Fisher Information Measure] minimization is equivalent to MaxEnt as a foundation for thermodynamics." "The realms of biology and astrophysics are usually regarded as distinct, to be studied within individual frameworks" say B.R. Frieden and B.H. Soffer at the beginning of Chapter 5, but "current searches for life in the universe, and the expectation of positive results, are guiding us towards a unification … called *astrobiology* … the unifying aspect of Fisher information is shown to form two bridges of astrobiology: (i) … quarter-power laws are found to describe both attributes of *biology*, such as metabolism rate, and attributes of the *cosmos*, in particular its universal constants. (ii) … the Lotka–Volterra growth equations of biology follow from quantum mechanics." Next, R.C. Venkatesan performs 'Encryption of covert information through a Fisher game' and A.L. Mayer, C.W. Pawlowski, B.D. Fath and H. Cabezas describe 'Applications of Fisher information to the management of sustainable environmental systems'. 'Fisher information in ecological systems' by Frieden and Gatenby complements this neatly. Finally, M.I. Yolles and B.R. Frieden "provide a framework, or paradigm, for estimating the logical past or future possibilities of a socioculture" in 'Sociohistory: an information theory of social change'. This begins with Kant's *noumenon* and Hegelian dialectic and a lot more along these lines until we reach 'A case illustration: postcolonial Iran', where the authors conclude that "for general constant growth rates and initial population levels the time as given at Eq. (9.18) defines a general state of parity of power. Beyond this time one faction becomes evermore powerful, indicating that the contest is over; consequently peace ensues. This scenario fits many former worldwide contests: The Ayatollahites vs Shahites, Axis powers vs Allies in WWII, USSR vs US, etc. Of course the peace we refer to may just mean physical non-violence, as opposed to structural non-violence from which social discontent may eventually follow. A corollary of these numerical results is that if an alliance balance is to be struck, the growth rates *must change* with time. In particular, these changes must be ever in the direction of balancing the two populations. For example, if population 1 is currently tending to dominate its growth rate must be diminished relative to that of population 2. These rate changes can of course occur naturally or be imposed from the outside (the 'third party' previously mentioned). If imposed, the art of achieving an alliance lies in continually adjusting them in the direction of Hegelian balance." By way of conclusion, the authors "emphasize *that the ultimate purpose of the mathematical approach is limited to providing a general framework*, or paradigm, from which the logical projections of stochastic possibilities for a socioculture can be clearly identified. The trends that are so identified can also help an inquirer to pose sensible new questions about sociocultural dynamics. These can, in turn, provide a structural aid to the inquiry process. For example, in this way 'What if …?' scenarios can be tested. The paradigm also acts in an unbiased manner, since it predicts likely outcomes without further partiality beyond the propositions created and their inconsummate interpretations." I had not come across 'inconsummate' before so looked it up in the OED, where the most recent quotation is dated 1695!

I did not realise when I reviewed the first four volumes of *Applied Scanning Probe Methods* that these were the first volumes of a saga and somehow missed the next three volumes of the tale. A further three have just appeared: volume VIII, *Scanning Probe Microscopy Techniques*, volume IX, *Characterization* and volume X, *Biomimetics and Industrial Applications* (the same sub-titles as the preceding batch), edited by B. Bhushan, H. Fuchs and M. Tomitori [32–34]. These are conceived as a single unit, the chapter numbering running from 1, "Background-free apertureless near-field optical imaging" by P.G. Gucciardi, G. Bachelier, S.J. Stranick and M. Allegrini at the beginning of volume VIII to 38, "Automated AFM as an industrial process metrology tool for nanoelectronic manufacturing" by T. Boo, D. Fong and S. Hand at the end of volume X. In between are contributions on such themes as "carbon nanotubes as SPM tips" by S. Marsaudon et al., "Scanning probes for the life sciences" by A.M. Ho and H.D. Espinosa, "Near-field optical spectroscopy of single quantum constituents" by

T. Saiki, "Gecko feet" by B. Bhushan and R.A. Sayer, "Carrier transport in advanced semiconductor materials" by F. Giannazzo, P. Fiorenza and V. Raineri, "Tissue engineering" by M. d'Acunto et al. and a great deal more. A further instalment is promised in a year or two.

Lastly, S.E. Tsimring on *Electron Beams and Microwave Vacuum Electronics* [35], which explores a very wide range of topics. In Part I, Electron Beams, the five chapters cover the 'Motion of electrons in external electric and magnetic static fields', 'Electron lenses', 'Electron beams with self fields', 'Electron guns' and 'Transport of space-charge beams'. Part II, Microwave Vacuum Electronics, likewise has five chapters, which go up to free-electron lasers. I naturally turned to 'Electron lenses', the chapter closest to ultramicroscopy, and was disappointed to find an old-fashioned and in some ways over-simplified account; the most recent book cited is that of Szilagyi (1988) and although I am of course delighted to see my *Magnetic Electron Lenses* (1982) among the references, it would be much more useful to cite Orloff's *Handbook of Charged Particle Optics* (1998—Tsimring cannot be blamed for not knowing that a revised edition will appear in 2008). An example of over-simplification is the account of the transfer matrix of a lens, which relates position and slope before and after the lens and has the general form

$$\begin{pmatrix} M & X \\ -1/f & M_\alpha \end{pmatrix}$$

where M denotes transverse magnification, M_α angular magnification ($=1/M$ for magnetic and einzel lenses) and f the focal length; X is zero if the matrix relates conjugate planes. I was therefore surprised to see

$$\begin{pmatrix} 1 & 0 \\ -1/f & 1 \end{pmatrix}$$

in Tsimring and had to look carefully to see that this applies to a thin lens, when the values of position and gradient are taken at the centre of the lens. The result is not wrong, of course, but is unhelpful. The transfer matrix is capable of conveying much more information than this, Further on, the author examines quadrupole lenses, and considers doublets and triplets, whereas the most interesting multiplet is the quadruplet, notably the so-called Russian quadruplet. The chapter ends with nine lines on 'Correction of aberration', which alas shows that the author is unaware of the developments of the last ten years.

7. Listings

A new edition of the *Handbook of Charged-Particle Optics* edited by J. Orloff should be available by the time you read this [36]. It is significantly different from the first edition of 1997, for not only have the contents been revised but a new chapter by O. Krivanek, N. Dellby and M.F. Murfitt on aberration-corrected electron microscopes has been added. The chapter on liquid metal ion sources by the late G.L.R. Mair has been revised thoroughly by R.G. Forbes and A.V. Crewe's account of STEM has been updated by P.D. Nellist. In addition to revising Mair's chapter, R.G. Forbes has written a new chapter on "Gas field ionization sources". There is, however, no longer a chapter on numerical methods; to compensate for this, J. Orloff has added an Appendix on Computational resources for electron microscopy but lecturers will miss the spectacular diagrams that they used to pirate for their courses. If you buy this, you will probably also add *Geometrical Charged Particle Optics* to your shopping list; H. Rose has at last completed his book on electron optics, due out early in 2009 [37]. More on all these next time as well as on the Proceedings of the 2006 Conference on Charged Particle Optics (CPO-7), to appear soon in the new open-access on-line serial from Elsevier, *Physics Procedia*.

Few electron microscopists will need to be told what "Williams and Carter" is; a new edition of this authoritative and extremely readable text [38] is also in press and will likewise be covered in detail next time. It is safe to predict that its sales will equal or surpass those of the 1996 edition.

Modesty usually forbids me from mentioning *Advances in Imaging and Electron Physics* here but I feel justified in drawing attention to volume 153, a thematic volume entirely concerned with aberration-corrected electron microscopy [39]. There are chapters on the correctors themselves by O. Krivanek and M. Haider and their associates and on applications of these new instruments by P. Batson (IBM), A. Bleloch (Super STEM), F. Houdellier, M. Hÿtch and others (Toulouse), B. Kabius and H. Rose (ANL and TEAM), A. Kirkland, P.D. Nellist and others (Oxford), S. Pennycook (ORNL), N. Tanaka (Tsukuba), K. Urban (Jülich) and Y. Zhu and J. Wall (BNL). The history of aberration correction is recounted by H. Rose. Volume 150 was also a special volume, with contributions by "star" authors: I. Daubechies, G. Teschke and L. Vese on image restoration with the aid of wavelets; J.M. Rodenburg on ptychography; and J. Serra on segmentation using mathematical morphology. A fourth chapter was a nice link with the past: the first long account of scanning electron microscopy appeared in these same Advances in 1965, written by C.W. Oatley, W.C. Nixon and R.F.W. Pease. The only survivor of the trio, Fabian Pease, describes developments in SEM in the period 1965–2007 [40].

Having overcome modesty once, I might as well continue: a second printing of *Science of Microscopy* [41] has been produced by Springer and this has made it possible to correct printing errors and also to use the blank space at the ends of chapters to mention the latest developments and include new references. Also from Springer is collection of articles on *Biological Low-voltage Scanning Electron Microscopy* edited by H. Schatten and J.B. Pawley [42].

Three titles from CRC Press (now part of Taylor & Francis) look of interest, though I have not seen the books themselves. First, *Introduction to Image Processing and Analysis* by J.C. and J.C. Russ, which, says the flier, "establishes the programming involved in image processing and analysis by utilizing skills in C compiler and both Windows and MacOS programming environments [43]. P. Campisi and K. Egiazarian have edited a collection of 10 essays on *Blind Image Deconvolution, Theory and Applications* [44]. Last in this group, *Introduction to the Principles of Materials Evaluation* by D.C. Jiles [45], which covers mechanical properties, acoustic and ultrasonic properties, thermal properties, electrical and magnetic properties, effects of radiation, mechanical, ultrasonic, electrical, magnetic, radiographic and thermal testing methods, destructive vs. non-destructive testing, defect detection and reliability and lifetime extension. An appendix provides solutions to the exercises. All this is squeezed into 272 pages.

Two books for French readers: *Nanosciences, la Révolution Invisible* by C. Joachim and L. Plévert [46] and, for French speakers rather than readers, *Comment ne pas endormir son auditoire en 30 secondes* by J.M. Aimonetti [47].

There has been a change in the publication of the proceedings of the two major Russian congresses on electron microscopy. Both sets used to appear in *Izvestiya Russ. Akad. Nauk (Ser. Fiz.)*, with an English translation a few months later in *Bull. Russ. Acad. Sci.* Now, however, only the general congress on electron microscopy appears in *Izvestiya/Bulletin*; moreover, the *Bulletin*, formerly published by Allerton Press, is now available from Springer and hence accessible via SpringerLink (lists of contents are on open access). However, do not forget that only a tiny subset

of the congress material finds its way into *Izvestiya/Bulletin*. Another useful addition to the web is the contents lists of *Izvestiya (Fizika)*, in both English and Russian, going back to vol. 68 (2004), at www.gpi.ru/izvestiyaran-fiz/content.htm. The most recent electron microscopy congress, the XXIst in the series, is to be found in *Izvestiya* 71 (10) (2007) [48]. Only 14 papers are included, among them two on miniature lenses by G.I. Fat'yanova and B.N. Vasichev, whom we also meet below; O.A. Podsvirov discusses "New aspects of dynamical electron diffraction in a crystal" and B.N. Grudin et al. describe "Methods of analysis of the structure of materials on the basis of orthogonal transformations of microscope images." I have seen only the titles and hence cannot give more details.

The proceedings of the other congress series, the Russian Symposia on Scanning Electron Microscopy and Analytic Methods of Studying the Solid State, now appear only in *Poverkhnost'* (where more extended proceedings of the earlier scanning meetings are also to be found). For the most recent congress, see Ref. [49]. Contents lists of *Poverkhnost'* can be found on http://www.issp.ac.ru/journal/surface/. Springer have recently begun publishing an English translation of *Poverkhnost'* entitled *Journal of Surface Investigation, X-ray, Synchrotron and Neutron Techniques* (ISSN: 1027–4510) but I have the impression that this is not a cover-to-cover version; two Russian issues make a single issue of the *Journal*. A Russian colleague has kindly sent me a copy of the 2006 issue of *Poverkhnost'* containing the Proceedings of the XIVth Russian Symposium. As usual, most of the papers are concerned with applications but there are two papers on instrumentation: G.I. Fat'yanova describes miniature magnetic lenses, quadrupoles and octopoles for multi-beam systems and in a companion paper, B.N. Vasichev and G.I. Fat'yanova show how these are assembled into complete electron-optical units.

The seventh seminar on Problems of Theoretical and Applied Electron and Ion Optics was held in May 2007 and the proceedings will be available as usual in *Prikladnaya Fizika* and a little later, in the SPIE Proceedings [50]. I have seen an "early copy" of the latter, and found many papers of ultramicroscopical interest. "A hybrid method of numerical calculation of magnetic systems with saturable materials" by D.E. Greenfield and A.P. Shulenok; "Computer simulation of field-emission multi-tip cathodes" by L.A. Baranova and G.M. Gusinsky; several papers on high current density beam optics; and two papers on beam-specimen interactions.

Several journals include congress papers. For the Proceedings of the 17th European Conference on Diamond, Diamond-like Materials. Carbon Nanotubes, Nitrides and Silicon Carbide (DIAMOND 2006), see *Diamond and Related Materials* [51]. APERIODIC 2006 is chronicled in *Phil. Mag.* [52].

8. Absent friends

Three microscopists whose names have occasionally figured in these columns have died recently and I felt that it would be nice to say a word about them here: Jim Barth, Nicolas Boisset and Giorgio Merli. Each was well known is his particular area of electron microscopy, though these did not overlap.

James Edmond Barth died suddenly on 18 February 2008 at the age of 72, still active in the Charged Particle Optics group of the Delft University of Technology. He was born in Mattoon (Illinois) in 1935, much the youngest of seven children as 12 years separated him from his closest sibling. He came to Delft in 1965 at the invitation of the late Prof. Dr Jan Le Poole and was involved in several of Le Poole's more unusual projects over the years; he and Le Poole were among the first contributors to *Ultramicroscopy*, with a recommendation to operate the electron microscope at 1–3 kV and an abstract in the Proceedings of the Grenoble ICEM (1970) records his contribution, with J. Kramer, to the folded TNO 1 MV electron microscope. Many papers on electron lens design appeared over the years; more recently, he had concentrated on gun optics and indeed, I still owed him a reply to a criticism of his! As Kees Hagen says, he was the "electron optics conscience." On the day of his death, he had attended the Dissertation defence of a PhD student and was cycling to a dinner, which he never reached. The subject of his own PhD, from the University of Arizona, was "Electrostatic correction of the spherical aberration of electron lenses" in which he studied the method of correction in which a fine gauze is placed in the path of the electron beam. Pieter Kruit recalls that "In the late eighties he initiated work on the computer optimization of electrostatic lens designs including engineering constraints, leading to a program that always came up with lower aberrations than the human lens designer. In the nineties, Jim produced his best cited and still generally used expression for 'the addition of different contributions to the charged particle probe size':

$$d_p = \left(\left(d_I^{1.3} + \left(d_A^4 + d_s^4 \right)^{1.3/4} \right)^{2/1.3} + d_c^2 \right)^{1/2}$$

with emphasis on the correct numerical prefactors for the individual contributions such as $d_s = 0.18 C_s \alpha^3$. His latest contribution appeared in print after his death: an analysis of the practical brightness of electron sources in *J. Vac. Sci. Technol.* B26 (2008) 949–955. At least as important as his contributions to the field were his contributions to the training of students, many of whom went on to build FEI's microscopes. He was always there to help them with the theory, point out flaws in their work or in the literature they were referring to. He was an extraordinary man who will dearly be missed by colleagues and students." Karel van der Mast, a close friend with whom Jim made a round-the-world tour in 1974 (Australia, New Guinea, Japan and the USA), has more personal memories: of making Jim learn to speak Dutch correctly; of many meals in the Chinese restaurants of Delft; of his violent reaction to the idea of eating doughnuts in Tokyo; of his relations with such visitors to Delft as Miklos Szilagyi, who expected students to line up outside his office to ask him for advice, and Harald Rose; of his religious convictions—he was a regular churchgoer; of his hospitality; the list could be much longer. An even closer friend was Mrs. Truus Groneman, Jan Le Poole's daughter, who remembers Jim arriving in Delft "for a short visit" after crossing the Atlantic by sea, "the only adventure he undertook in his life." His first small room had no shower and Jim was a regular visitor to the Le Poole's home (and their bathroom). Jim was able to return this service some years later, by which time he was living in a flat with a bath, unlike Truus Groneman and her three children: they (and any visiting children) used *his* bathroom before he returned home from the laboratory—but not always: "One day, I had five naked kids in front of the TV and in came Jim. Once again, he remained imperturbable and made us tea and lemonade." After Jan Le Poole's retirement, Jim talked about returning to the USA but he was too deeply rooted in the Delft atmosphere. Truus Groneman was not present at the dinner he gave for all his colleagues on his 65th birthday. "'Did I miss an entertaining evening?', I asked. 'Of course not', he replied, 'The best horse in the stable could choose!' That was the first time he said anything affectionate and together we went to a restaurant." After that, he no longer contemplated leaving Holland. Each year, he spent several weeks with his remaining family in Mattoon and he had indeed been there not long before his death; two of his sisters are still alive, Ruth who is 88 and Mary Frances, 93. Truus Groneman accompanied the body to the United States, where Jim was interred in the family grave, with

his parents and three brothers. "We all liked him and he will be much missed."

Pier Giorgio Merli was only 65 when he died suddenly on 23 February 2008; he was Director of Research at the CNR Istituto per la Microelettronica e i Microsistemi (IMM, formerly LAMEL-CNR) in Bologna, of which he had been Director from 1992 to 1998; he was President of the Italian Society of Electron Microcopy (SIME) from 1984 to 1987. I think that he would have liked to be remembered for his early experiment of 1972 with Gian Franco Missiroli and Giulio Pozzi, also of the University of Bologna, on electron interference, in which Young's interference fringes could be seen gradually emerging from noise as single electrons arrived at the detector—the film won a prize at the International Festival on Scientific Cinematography in Brussels (1976). His interests were wide, however; in SEM, for example, he contributed to our understanding of the image-forming mechanism and also delved into the history of the instrument. His friends will know that his human qualities more than matched his scientific merits and I cannot do better than quote a tribute by one of his colleagues: "He was a scientist and, beyond that, a rigorous and passionate intellectual, one never completely satisfied with the acquired knowledge, always aiming at a deeper and more refined level of understanding. Aware of his role as an intellectual, he was honest and disinterested, always seeking to be consistent and transparent in his professional and human relationships. His coherence reflected a belief in morality, equity, and merit." Like Jim Barth, much of his time and energy was given to undergraduate and graduate teaching, for he regarded the transmission of knowledge and, above all, intellectual standards as paramount.

Nicolas Boisset, born on 3 June 1963, was much younger than Jim Barth and Giorgio Merli when he died on 4 January 2008. He had recently been elected President of the French Microscopy Society and during a meeting of the Council of the Society, announced that he would be unable to continue, a brave and moving declaration: in the summer of 2007, he had been told that he had only six months to live. His professional life was spent in the world of three-dimensional reconstruction, first in Tours, in the laboratory of Jean Lamy, where he had an office in the Fondation Paul Metadier (now demolished) and later, when the situation in Tours became uncertain, in the Institut de Minéralogie et de Physique des Milieux Condensés, Campus Boucicaut, in Paris, where he was Director of Research (CNRS). He twice visited Joachim Frank's laboratory in Albany, for nearly two months in 1985 and for three months in 1988; Joachim Frank, who was a member of his thesis jury in 1990, writes "Nic was one of the students I was most proud of. Once he had left Tours, he established a lab in Paris which produced solid results and enjoyed an international reputation. One of his students, Magali Cottieiville, has joined my lab last year as he was struck with his disease. Notwithstanding the significance of his contributions in some areas of biology, his most visible legacy is probably a set of most carefully prepared didactic slides explaining the different steps of image processing, which have found their way into many text books and training manuals on cryo-EM. In a paper shortly to come out in *Nature Protocol* (Shaikh et al., 2008), coauthored by Nic and now dedicated to his memory, some of these images are reproduced as a means of introducing the most important concepts of single-particle reconstruction." His close friend, Sergio Marco (SM below), has sent me many memories of Nicolas, beginning with their first meeting in Tours, where SM applied for a post as university lecturer. The laboratory was spread over two buildings, the Faculty of Medicine and the basement of the Fondation Metadier; "It was in the latter that Nicolas hid (I choose the word deliberately) in a small ill-lit office, which led into a room containing an evaporator and other specimen-preparation material, a dark-room and the electron microscope room. Nicolas was alone there, in the calm, which seemed to suit him, together with boxes of carefully classified reprints." They spent the afternoon together, discussing the purchase of a modern electron microscope and visiting the city of Tours before SM returned to Madrid, where he was at that time working in Jose L. Carrascosa's laboratory. Nicolas Boisset had spent some time in Joachim Frank's laboratory in Albany (NY) and one of SM's first tasks after taking up his post in Tours was to master the SPIDER software that Nicolas Boisset had brought back with him from Albany. SM was struck by the isolation of Nicolas from the remainder of the laboratory and, as relations with Lamy cooled, their friendship deepened: Nicolas came to the birthday party of SM's little daughter. But "The situation was becoming critical: the Metadier building was due to be demolished, the university no longer supported the microscope project and on a more personal level, Nicolas Boisset's mother was taken seriously ill. A new research group sprang up around J.C. Taveau (who soon moved to Bordeaux) but Nicolas felt that he did not fit in and the outcome was that he moved to Paris, to be followed by SM." They were not, however in the same laboratory as SM was attached to the Institut Curie, first in Paris but later at Orsay. Things jogged along, catalysed by Carrascosa's invitation to join the European Network 3DEM, in which Nicolas would concentrate on single-particle reconstruction and SM on electron tomography. "Then, one day, Nicolas phoned me and said that we must have a quiet talk together as he had developed cancer and had been given only six months to live by his doctors. This was in the summer of 2007. He asked me to tell no-one and to help him to depart in peace, leaving everything in good order. He kept his worries to himself but after a long discussion, I urged him to be treated at the Institut Curie, which was not only a good hospital but would bring him into contact with Daniel Lévy, with whom I shared a laboratory. His first stay in hospital passed off well but he was aware that time was running out; he knew what to expect for other members of his family had suffered the same fate, and he did not want chemotherapy. Another friend, Eric Larquet, and I tried to make him change his mind but he remained firm, his only family was a nephew and, a convinced Catholic, he believed in an after-life. Then, probably to enable him to finish putting his affairs in order, he did accept chemotherapy but the treatment exhausted him and he returned to hospital for a while, where he continued to work on the 3DEM project and reflected on his position in the French Microscopy Society, of which he was President-Elect. In December 2007, Eric Larquet phoned me to say that Nicolas was back in hospital. We knew that the end could not be far off. I returned to Madrid for Christmas with my family and I am convinced that Nicolas struggled to hold on until the Christmas season was over, dying when everyone was back at work, peacefully, discreetly, without disturbing anyone."

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Corrosion Casting Conference 2008

28 ottobre 2008, Varese

Il 28 ottobre scorso si è tenuta nel campus universitario di Varese la "Corrosion Casting Conference 2008", organizzata congiuntamente dal Dipartimento di Morfologia Umana e dal Dipartimento di Chirurgia della Università degli Studi dell'Insubria, nel quadro delle manifestazioni per il decennale della fondazione dell'Università.
Quella dei calchi vascolari (corrosion casts) è una tecnica di preparazione preliminare all'osservazione al SEM che permette di osservare la struttura del microcircolo e del relativo endotelio in tre dimensioni con una risoluzione molto elevata. D'altra parte è una tecnica delicata e complessa, che pochissimi ricercatori hanno portato a livelli di reale eccellenza.
La manifestazione, rivolta a tutti i ricercatori e i dottorandi interessati alla morfologia del microcircolo ed in particolare ai fenomeni neo-angiogenetici neoplastici, è stata inaugurata da una relazione introduttiva di A. Lametschwandtner (Salisburgo) e si è poi articolata in sei *lectures* con la partecipazione di quasi tutti i maggiori esperti di questa tecnica in Europa. S. Sangiorgi e T. Congiu (Varese) hanno esposto i dettagli tecnici del corrosion cast, mentre E. Mayer ed A. Ulmann-Schuler (Zurigo) hanno presentato una interessante variante di questa tecnica. S. Cotrufo (Glasgow) ha illustrato le applicazioni del corrosion cast nella messa a punto di nuove tecniche in chirurgia ricostruttiva, ad altre applicazioni cliniche sono state presentate da D. Kachlik (Praga). A. Manelli (Imperia) e M. Raspanti (Varese) hanno infine esposto alcune applicazioni grafiche avanzate per la visualizzazione tridimensionale dei calchi vascolari.

Da questa prima Corrosion Casting Conference trae origine il corso teorico-pratico "Tecnica ed applicazioni dei calchi vascolari (corrosion cast)", che si terrà nel 2009 sotto l'egida della Società Italiana di Scienze Microscopiche.

Mario Raspanti

Nella foto, il line-up dei relatori. In piedi da sinistra Eric Mayer, Alexandra Ulmann-Schuler, Alois Lametschwandtner, Stefano Cotrufo e Mario Raspanti. In basso da sinistra David Kachlik, Simone Sangiorgi ed Alessandro Manelli.

Eventi nazionali

Segreteria scientifica

Rosemarie Heyn ***(Ref.)***
Irene Faenza
Ebe Parisi
Rosa Vaccaro
Antonio Musarò

Segreteria tecnica

Gianfranco Franchitto ***(Ref.)***
Anna Andreani
Giuseppina Trecina
Luciano Sbraga

Eventi nazionali

congressosiai2009@ircc.it

SIAI 2009

Il 63° Congresso Nazionale della Società Italiana di Anatomia e Istologia si terrà a Torino dal 10 al 12 settembre 2009 presso il Centro Congressi Torino Incontra, strategicamente situato nel centro della città storica. Il Congresso si terrà all'insegna della tradizione con qualche innovazione: una sessione inaugurale, due relazioni, una lettura magistrale plenaria, dodici sessioni parallele tematiche e due sessioni di posters. Al fine di allocare gli spazi e di organizzare i tempi e le tematiche relative alle varie sessioni la scadenza per la presentazione di "abstracts" e' fissata per il giorno 1 maggio 2009. E' possibile effettuare la registrazione "on line" (questo sito), indicando il settore o tema di ricerca oggetto della presentazione.

Parallelamente al Congresso della Societa' di Anatomia e Istologia si svolgeranno il 2009 EMBO Molecular Medicine Workshop avente per oggetto "La crescita invasiva: un programma genetico per le cellule staminali e il cancro" nonchè un mini-simposio satellite nell'ambito del Programma Europeo "Microambiente e Metastasi". La partecipazione a entrambi gli eventi e' libera e gratuita per gli iscritti al Congresso SIAI 2009.

Eventi internazionali

Microscopy Conference 2009 in Graz MC 2009 Graz

30 August – 4 September 2009

Congress Graz, Austria

Joint Meeting of

9th Multinational Congress on Microscopy 2009

- Austrian Society for Electron Microscopy
- Croatian Microscopy Society
- Czechoslovak Microscopy Society
- Hungarian Society for Microscopy
- Italian Society of Microscopical Sciences
- Serbian Society for Microscopy
- Slovene Society for Microscopy

&

Dreiländertagung 2009

- Austrian Society for Electron Microscopy
- German Society for Electron Microscopy
- Swiss Society for Optics and Microscopy

www.microscopy09.tugraz.at

30 August – 4 September 2009
Congress Graz, Austria

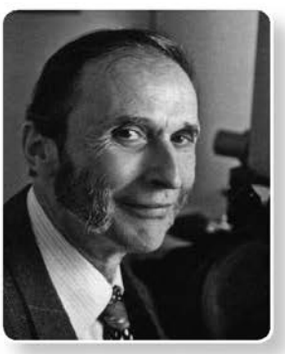
MC 2009 Graz

Ladies and gentlemen, dear colleagues,

With great pleasure we like to announce the Microscopy Conference 2009 in Graz (30 Aug–4 Sept 2009). MC 2009 is joining up the «Multinational Congress on Microscopy» and the «Dreiländertagung» both having established a strong reputation as key events of the European and international microscopy communities.

The programme committee is setting up a scientifically stimulating, future oriented programme in the three main areas of instrumentation and methodology, materials science and life sciences. The programme comprises plenary lectures, keynote lectures, poster sessions, symposia and workshops. Special emphasis is given on the importance of the poster sessions, which means, considerable time will be allocated to the presentations and discussions of the posters. During the whole conference there will be a high quality Trade Exhibition in the same building adjacent to the lecture halls displaying modern instruments and state-of-the-art developments in microscopy of the physical and life sciences and nanotechnology. Together with the exhibitors' presentations this will be another highlight of the conference.

We have been trying to keep the conference fee low; especially for students the reduced conference fee will be € 80 only. Therefore we kindly ask you to encourage young scientists to present their contributions to make this meeting an even more lively event. As a special offer to our international colleagues being members of other microscopical societies we would like to invite you to register at the reduced rates as they are valid for the members of the organizing societies.
We really want you all to feel at home at MC 2009 in Graz.



We are pleased to host the meeting in Graz hoping it will be a landmark. Graz is a city in the centre of Europe that has a long history in science, engineering and culture. The venue of the conference is a historical building located right in the centre of the city, equipped with modern conference facilities.

To receive further information please contact us at:
www.microscopy09.tugraz.at

Again, we would like to invite you to participate and make this conference by your contributions a scientifically stimulating and fruitful meeting of people developing and using modern microscopical methods. We are looking forward to seeing you all at MC 2009 in Graz.

Yours sincerely,

H. Peter Karnthaler
President of the MC 2009 Graz

www.microscopy09.tugraz.at

Microscopy Conference 2009 in Graz

International Scientific Advisory Board

- Marie Cheynet (Grenoble)
- Christian Colliex (Paris)
- Aleksandra Czyrska-Filemonowicz (Kraków)
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- Ferdinand Hofer (TU Graz, Chairman)
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- Manfred Leisch (TU Graz)
- Maria-Anna Pabst (MU Graz)
- Peter Pölt (TU Graz)
- Günther Zellnig (KFU Graz)

www.microscopy09.tugraz.at

30 August – 4 September 2009
Congress Graz, Austria

MC 2009 Graz

Congress Topics

Instrumentation and Methodology

- Atomic resolution microscopy (aberration correction, phase retrieval, holography)
- Scherzer symposium on advanced electron optics (detectors, phase plates, spectrometers,monochromators) to commemorate the 100th birthday of Otto Scherzer
- 3D-Imaging, nanotomography (Dual Beam, ultramicrotomy, …) incl. data reduction
- Analytical TEM (EELS, EFTEM, X-rays)
- SEM (X-rays , STEM, low vacuum, low energy, …)
- Other current topics of microscopy (atom probe, scanning probe, …)

Life Sciences

- 3D and Cryo-TEM
- Confocal microscopy, correlative fluorescence and electron microscopy
- Intracellular trafficking and cellular dynamics
- Plant sciences
- Microscopy in developmental biology and medicine
- Structures of cells and tissues, and localization of molecular targets (LM, EM, AFM)
- Other current topics of Life Sciences

Materials Science

- Materials for information technology
- Nanoparticles
- Alloys and intermetallics
- Ceramics, coatings, geomaterials, …
- Carbon based materials, soft materials, polymers
- Thin films and interfaces
- Other current topics of Materials Science

www.microscopy09.tugraz.at

30 August – 4 September 2009
Congress Graz, Austria

MC 2009 Graz

Information

Location
Graz, the capital of Styria, lies at the heart of Europe. A major university city, it is also a vibrant centre of the arts, science and research – and business. With a population of about 280,000, making the largest conurbation in Styria, the greater Graz area plays a leading role in technology.

Accommodation
Hotels of a wide range, from standard to luxury, are available in walking distance of Congress Graz and can be booked via the conference website. Special arrangements for student accommodation will be made.

Congress Venue
The venue of the meeting will be Congress Graz, located in the beautiful historic city centre of Graz featuring halls and rooms with a total of 2,900 square metres.
www.grazercongress.at

Climate
Sub alpine climate, warm days and fresh nights in summer.

Travel
Graz can be easily reached by train from within Austria, Slovenia, Italy and Hungary. The international airport Graz is directly connected to Frankfurt, Berlin, Düsseldorf, Munich, London, Zürich&Vienna.

Important Dates
- **Abstract submission and registration open**
  15 January, 2009
- **Abstract submission deadline**
  15 April, 2009
- **Early registration deadline**
  30 April, 2009
- **Hotel reservation deadline**
  31 July, 2009

Conference Language
English

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Eventi internazionali

Focus on Microscopy 2009
Krakow, Poland
April 5 - April 8, 2009

Dear colleagues,

After the this years successful conference in Osaka/Awaji (group picture), Japan we like to announce the next conference in the FOM series. It will take place in Krakow, Poland from Sunday April 5th to Wednesday April 8, 2009. Please note that this is in the week before Easter 2009. The conference excursion and dinner will take place on the afternoon/evening of the last day of the conference, 8 April.

The conference will take place at the Jagiellonian University in the center of Krakow. Details of registration, abstract submission, deadlines, etc. will become available at a later moment on this website. When you wish to be kept informed please leave your email address here.

Focus on Microscopy 2009 is the continuation of a yearly conference series presenting the latest innovations in optical microscopy and their application in biology, medicine and the material sciences. Key subjects for the conference series are the theory and practice of 3D optical imaging, related 3D image processing, and reporting especially on developments in resolution and imaging modalities. The conference series is covers also the rapidly advancing fluorescence labeling techniques for the confocal and multi-photon 3D imaging of -live- biological specimens.

Typical topics of the upcoming FOM conference will include:

• Confocal and multiphoton-excitation microscopies • Novel illumination and detection strategies • Fluorescence - new labels, fluorescent proteins, quantum dots, single molecule • Time-resolved fluorescence - FRET, FRAP, FLIM, FCS • Coherent non-linear microscopies - SHG, THG, SFG, CARS • Raman, light scattering microscopy • Multi-dimensional imaging • Sub-wavelength resolution - near field microscopy, STED, PALM • Laser manipulation, ablation and microdissection, photoactivation • Optical tools in genomics, proteomics, phenomics, cytometry • Magnetic resonance and X-ray microscopy • Image processing and visualisation • Live cell and whole tissue imaging

A technical exhibition will be a feature of the Krakow FOM2009 conference.

The programs of the previous FOM conferences from 2004 onwards together with the page abstracts of contributions can be viewed in PDF format on this website by clicking the History button on the left.

Welcoming you to the Krakow FOM2009 conference and exhibition,
On behalf of the FocusOnMicroscopy society,
- Jurek Dobrcuki, Jagliellonian University Krakow, Poland
- Fred Brakenhoff, University of Amsterdam, The Netherlands

The FOM2009 conference incorporates the
- 22nd International Conference on 3D Image Processing in Microscopy
- 21th International Conference on Confocal Microscopy

Eventi internazionali

EDGE 2009: International EELS-Workshop

May 17 – May 22, 2009
Banff, Alberta, Canada
www.banffcentre.ca

This web site covers a series of workshops in the field of electron energy-loss spectroscopy.
The first was at Lake Tahoe in 1990, while the most recent one was held in 2005 at Grundlsee in Austria.
More information about the next meeting please click here.

For questions and additional information, please contact:

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Eventi internazionali

EBSA 2009

European Biophysics Congress Genoa
11th - 15th July 2009 Genoa, Italy

EBSA
Biophysics in Europe

Welcome to the website for the 7th European Biophysics Congress, organised under the auspices of the European Biophysical Societies Association (EBSA) and the Italian Society for Pure and Applied Biophysics (SIBPA).

The **EBSA 2009 meeting** is scheduled for **July, 11th-15th 2009 in Genova, Italy** and is intended for scientists and students from academia, industry, government and higher education.

This site provides information on the location of the Congress and the Scientific Sessions, the congress dinner, the Organising Committee and the Scientific Committee. You can also find details about accommodation and abstract submission. Please, check this website regularly for updates.

Important congress dates

- **Welcome and Opening Lecture: July 11th 2009**
  - ***Opening Ceremony: 5.30p.m.***
  - ***Opening Lecture: 6p.m.***
  - ***Welcome Party: 7p.m.***
- **Congress Dinner: July 13th 2009**
- **Early registration deadline: April 30th 2009**
- **Abstract submission deadline: April 7th 2009**

Special Scientific Events

- **A scientific session will be dedicated to Antonio Borsellino.**
- **A scientific session will be dedicated to Poster awards.**

Other Events and concessions

- A Night at the Opera
- City lights tour
- City Museums pass
- Public transport facilities
- Social dinner
- Commercial Exhibition

Conference information

diaspro@ebsa2009.org (subject: W-EBSA2009)

EBSA Biophysics in Europe

SIBPA Società Italiana di Biofisica Pura e Applicata

UNIVERSITÀ DEGLI STUDI DI GENOVA

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Springer the language of science

European Biophysics Journal with Biophysics Letters

Eventi internazionali

21st Nuclear Workshop

21-st Wilhelm Bernhard Nuclear Workshop

31.08 - 04.09.2009 Ustroń, Poland

Dear friends and colleagues,

We have the pleasure to announce the organization of the next Wilhelm Bernhard Workshop. The 21st International Workshop on the Cell Nucleus will be held in Ustron, Poland, from the 31 August to the 4 September 2009. Ustron is a charming small resort in the Beskidy Mountains 60 km south from Katowice, the capital of the Silesia district.

The Wilhelm Bernhard Workshop is a biennial event focusing on functional and structural aspects of the nucleus and its component structures. The Workshop fosters interaction and cooperation between scientists from all parts of the world and especially encourages the active participation of young scientists. The major aim of the Workshop is to create a multidisciplinary meeting representing most research approaches used in studies on the cell nucleus structure, functions, and their relationships, as well as to give young scientists the opportunity to present their research within a fairly small circle of competent colleagues and to meet experienced colleagues in their field of research.

We hope to see you in Ustron!

Eventi internazionali

1st INTERNATIONAL SYMPOSIUM OF CLINICAL AND APPLIED ANATOMY

18 - 19 SEPTEMBER 2009, NOVI SAD, SERBIA

INVITATION

It is our great pleasure and honour to invite you to the "***1st International Symposium of Clinical and Applied Anatomy***", that will take place in Novi Sad between 18–19 September 2009. We will do whatever we can to achieve optimal surrounding for a scientific happening. We are also convinced that the Symposium and the city of Novi Sad will be a unique meeting place of dear friends and colleagues. Within the medical profession, we are celebrating fifty years of existence and development of Department of Anatomy, Faculty of Medicine in Novi Sad.

Novi Sad is located in the southern part of Europe, in Serbia, about 80 km north-west from Belgrade and it lies on the left bank of the river Danube. It is the second largest city in Serbia. It is hard, if not impossible, for us, the citizens of Novi Sad, to talk about our city or to show its pictures in an impartial way, without showing how much we love it and how much we are struggling to remain worthy of its past. It is a city one gets to know and love easily, but also a place hard to forget and leave forever. Novi Sad is a University city, hospitable and open-hearted to all of its visitors, built by measure of a man.

We await your answer and we are looking forward to seeing you in Novi Sad in September 2009.

First announcement follows until 15th February 2009.

Yours faithfully,
Radmila Gudović, MD, PhD

President of the Symposium Organisation Committee

Contact:

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Eventi internazionali

e-mail contact: ciasem2009@cab.cnea.gov.ar

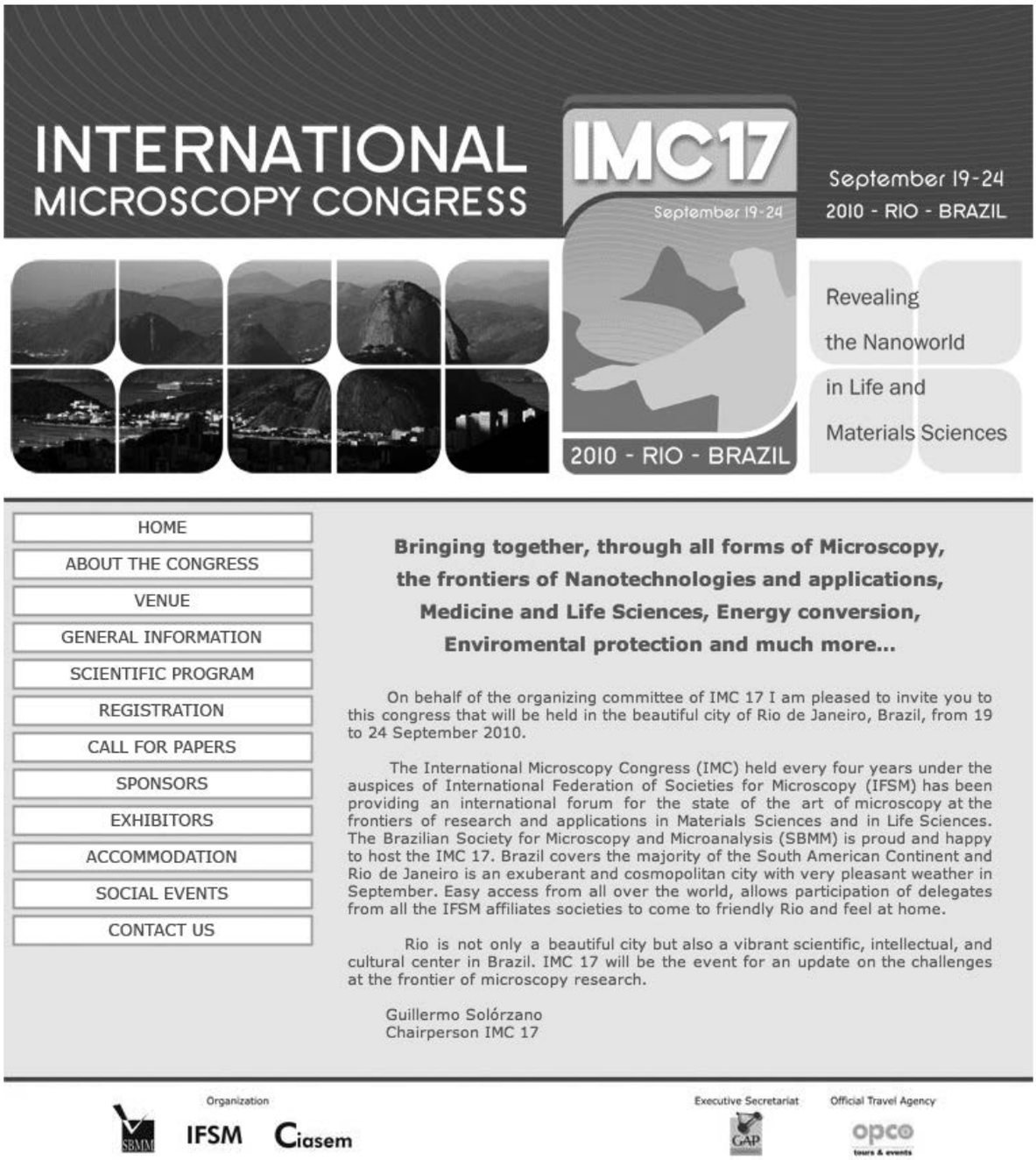
Welcome

In October 2009, the 10th Inter-American Congress on Electron Microscopy (CIASEM 2009) and the 1st Congress of the Argentine Society of Microscopy (SAMIC 2009) will be held jointly in Argentina, in the city of Rosario.

The CIASEM Congresses are held every two years, and are the largest and most important meetings on electron microscopy and microscopies throughout the Americas. They have previously been held in Brazil, Ecuador, Mexico (twice), Venezuela (twice), United States of America, Cuba and Peru.

These congresses are sponsored by CIASEM, the Inter-American Committee of Societies for Electron Microscopy, a regional organization of IFSM, the International Federation of Societies for Microscopy, for the Western Hemisphere.

Eventi internazionali



Consorzio M.I.A. - Microscopy and Image Analysis. Consorzio per lo sviluppo della microscopia e dell'analisi d'immagini nella ricerca biomedica e tecnologica

Facoltà di Medicina e Chirurgia dell'Università di Milano-Bicocca, Via Cadore 48, 20050 Monza, Italy

Presidente del Consorzio: Prof. Emilio Berti
Direttore del Consorzio e responsabile laboratorio: Dott. Antonello Villa. E-mail: antonello.villa@unimib.it

Il Consorzio M.I.A. continua un'esperienza cominciata alla metà degli anni novanta per iniziativa dell'Università degli Studi di Milano e dell'Ospedale S.Raffaele di Milano, come Open Laboratory M.I.A., all'interno del DIBIT HSR.

Attualmente i Soci del Consorzio sono:
- Università degli Studi di Milano-Bicocca;
- Istituto di Ricerche Farmacologiche Mario Negri;
- Fondazione IRCCS Istituto Nazionale dei Tumori;
- Fondazione M. Tettamanti;
- Fondazione Matarelli;
- Fondazione D'Amico.

Sono in corso trattative per l'ingresso di nuovi Soci.

Il Consorzio è senza fine di lucro e deve tendere all'autosufficienza della gestione. Eventuali avanzi di gestione devono essere reimpiegati nelle iniziative che formano oggetto della sua attività.

Gli Organi Consortili previsti dallo Statuto sono i seguenti:
- Presidente;
- Direttore;
- Consiglio di Amministrazione (in cui sono rappresentati tutti i Soci);
- Assemblea dei Soci;
- Comitato Tecnico Scientifico (composto da 9 specialisti di diverse discipline, presieduto dal Prof. Adalberto Sessa).

Gli obiettivi per cui è stato costituito il Consorzio, in gran parte coincidenti con quelli dell'Open Lab M.I.A., sono:
- creare un laboratorio in grado di collaborare scientificamente, offrendo supporto tecnico-scientifico in campo morfologico, sia con gli Enti afferenti sia con gruppi di ricerca esterni, su progetti approvati dal Comitato Tecnico Scientifico (CTS);
- garantire consulenza nelle diverse tecniche morfologiche a chiunque ne faccia richiesta;
- garantire lo sviluppo delle tecniche e delle tecnologie al fine di fornire un supporto morfologico sempre all'avanguardia;
- razionalizzare gli investimenti per acquisire strumentazioni ed introdurre tecniche e tecnologie che sarebbero troppo onerose per un unico Socio
- creare un ambito che permetta la crescita e la formazione di nuovo personale qualificato.

Tutti i progetti in collaborazione devono essere preventivamente valutati e approvati dal Comitato Tecnico Scientifico del Consorzio tenendo conto solo della loro qualità e fattibilità.

Grazie anche al buon lavoro di selezione del Comitato, dal 1995 ad oggi il personale del M.I.A. ha collaborato con decine di gruppi di ricerca differenti, offrendo loro supporto morfologico, contribuendo alla pubblicazione di oltre 60 lavori, con un Impact Factor medio superiore a 9.0. L'elenco completo delle pubblicazioni, assieme allo Statuto ed a tutte le informazioni utili per conoscere meglio la realtà del Consorzio, si può trovare visitando il sito web all'indirizzo: *www.consorziomia.org*.

Nonostante quanto detto sinora possa far pensare ad un grande laboratorio estremamente attrezzato ed organizzato, con molto personale e molte risorse, la realtà del Consorzio M.I.A. è ancora piccola, sebbene con buone prospettive di crescita.

Il Consorzio è stato fondato a Monza nel 2002 dopo la fine dell'esperienza dell'Open Lab. M.I.A decretata dalla modifica dei rapporti fra l'Università degli Studi di Milano e l'Ospedale S. Raffaele.

Il laboratorio del Consorzio è partito in pratica da zero, potendo contare solo su una consolidata esperienza, un buon numero di collaborazioni e qualche borsa di studio.

Determinante per l'inizio delle attività del Consorzio presso la Facoltà di Medicina e Chirurgia dell'Università di Milano-Bicocca è stata la disponibilità a collaborare dimostrata da alcune aziende del settore (soprattutto Bio-Rad, Emme3,

FEI Italia, Leica Microsystems, Nikon Instruments, e Media System) che hanno messo a disposizione, a condizioni economiche favorevoli, gran parte delle attrezzature "essenziali". Nei primi anni di vita del Consorzio gli investimenti, certamente anche a causa del difficile momento che la ricerca italiana sta attraversando, sono stati veramente limitati e hanno permesso di acquisire solo parte delle apparecchiature e delle tecniche previste al momento della fondazione.

In questo momento, grazie alla strumentazione a disposizione, il supporto morfologico offerto riguarda la microscopica ottica, confocale, elettronica a trasmissione ed a scansione, con particolare attenzione alle tecniche di immunolocalizzazione, anche a livello ultrastrutturale. L'esperienza acquisita permette di consigliare la tecnica più adatta ad affrontare i differenti problemi (Figura 1). Fortunatamente gli ultimi mesi sono stati caratterizzati da alcune importanti novità che ci permettono di guardare con ottimismo al futuro.

Innanzitutto l'apertura presso il "nuovo" Istituto Mario Negri, Socio fondatore del Consorzio, di un laboratorio di morfologia ultrastrutturale ben attrezzato affiliato al Consorzio M.I.A. (responsabile il Dr. Fabio Fiordaliso).

La chiusura del laboratorio di microscopia elettronica dell'Istituto Nazionale dei Tumori di Milano e la conseguente donazione delle attrezzature al Consorzio ha consentito, come era già avvenuto precedentemente per la chiusura del laboratorio morfologico della Fondazione Matarelli, di potenziare le attrezzature del laboratorio di Monza.

Il 2009 inoltre si è aperto con l'assegnazione al Consorzio, da parte dell'Università di Milano-Bicocca, di un'unità di personale tecnico e l'assunzione, direttamente da parte del laboratorio del Consorzio, del primo ricercatore.

La peculiarità del Consorzio, che ne rappresenta la vera "forza", è la massima apertura a collaborare con chiunque presenti un progetto di ricerca valido, indipendentemente dall'argomento e dall'affiliazione del gruppo proponente.

La filosofia del M.I.A è sempre stata quella di collaborare con gli altri, prendendo stimolo dai

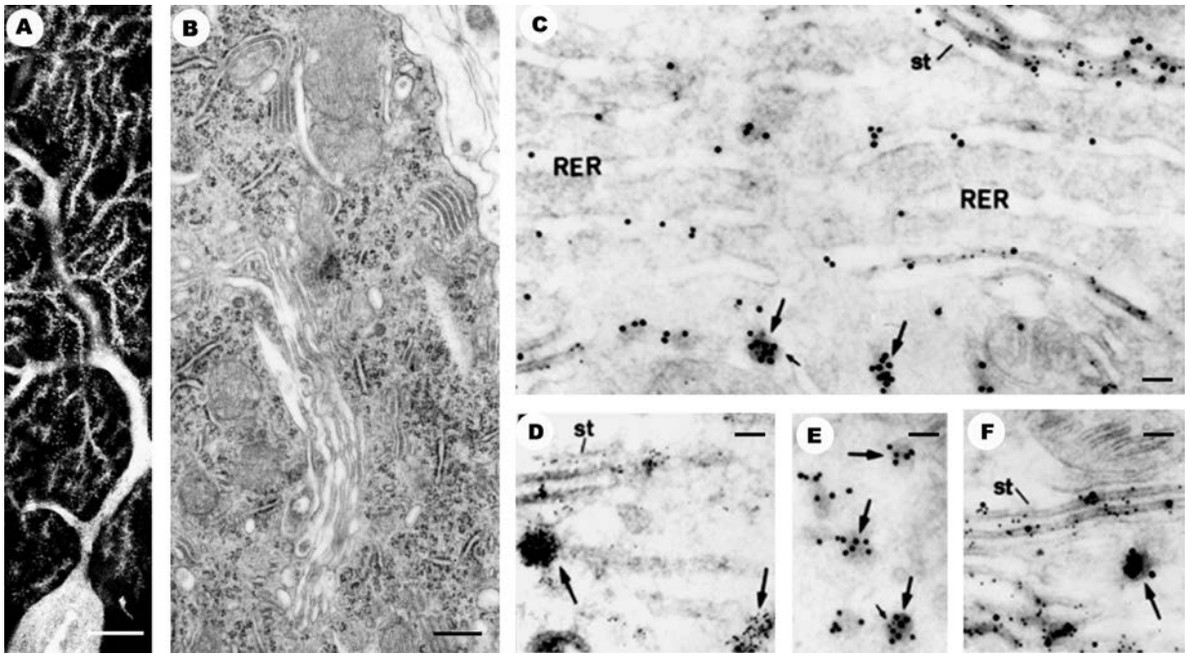


Figura 1. Cervelletto di ratto: cellule del Purkinje osservate con diverse tecniche morfologiche. A) Microscopia confocale: immunolocalizzazione di Calsequestrina. B) Microscopia elettronica a trasmissione di sezioni ultrasottili di tessuto incluso in resina epossidica. C,D,E,F) esempi di immunolocalizzazione, con oro colloidale su criosezioni ultrasottili, di proteine coinvolte nella regolazione del Calcio intracellulare.
Barra d'ingrandimento: A) 10 μm B) 300 nm C,D,E,F) 100 nm.

problemi che i diversi progetti presentano, per sviluppare od introdurre nuove tecniche e tecnologie al fine di risolverli adeguatamente.

La grande eterogeneità dei problemi scientifici affrontati in questi anni, documentata dai lavori pubblicati, dimostra chiaramente la varietà delle richieste pervenute. L'ultima riunione del Comitato Tecnico scientifico ha preso in esame 31 richieste di collaborazione provenienti da 16 gruppi di ricerca di 13 enti differenti. Nel 2008 nei laboratori del M.I.A. sono stati portati avanti esperimenti inerenti a 15 diversi progetti. Buona parte di questi riguarda problematiche oncologiche come, ad esempio, lo studio di microvescicole rilasciate dalle cellule tumorali umane e del loro ruolo modulatorio nei confronti del sistema immunitario (Figura 2) oppure la caratterizzazione di 'putative stem cells'. Sempre sul tema delle cellule staminali, il laboratorio si sta occupando dell'utilizzo di cellule staminali mesenchimali umane, deposte su scaffold in idrossiapatite, con lo scopo di esplorare il loro uso nella terapia rigenerativa delle pseudoartrosi atrofiche (Figura 3). Contemporaneamente il laboratorio si occupa anche del ruolo di "nuove" proteine coinvolte nella formazione di complessi giunzionali e, in collaborazione con la Banca degli occhi, dell'analisi ultrastrutturale di cornee umane prelevate con diverse tecniche.

Il numero di richieste di collaborazione e l'Impact Factor medio delle pubblicazioni dimostrano chiaramente sia il buon lavoro di selezione fatto dal CTS sia il fatto che il Consorzio sta rispondendo ad una reale esigenza espressa da molti Ricercatori del nostro Paese. I risultati sin qui raggiunti provano che la filosofia seguita è redditizia, almeno sul piano scientifico, sebbene sia anche alla base di alcuni problemi, ad esempio quelli derivanti dalla difficoltà di approfondire adeguatamente i "troppi" temi trattati e quindi la mancanza di esperienza specifica in un campo preciso della ricerca, se non genericamente in quello tecnico morfologico.

Spaziare dall'oncologia alle neuroscienze (Figura 4), dall'ortopedia alla nefrologia, da problematiche strettamente di "ricerca di base" a quelle di "ricerca clinica", crea serie difficoltà anche nell'acquisizione di finanziamenti, poiché i bandi richiedono spesso una comprovata specializzazione.

Anche per questa ragione, pur essendo il Consorzio M.I.A., per Statuto, senza fine di lucro, si è deciso di mettere a disposizione l'esperienza e la professionalità acquisita offrendo un servizio a pagamento ad aziende, enti ed istituti che operano anche in campi diversi da quello biomedico.

Fra l'altro sono state aperte trattative per fornire un supporto ultrastrutturale ad Aziende Ospedaliere a fini diagnostici. La competenza del Consorzio è soprattutto qualificata nella valutazione ultrastrutturale delle lesioni che caratterizzano diverse patologie renali. Specializzazione particolarmente rilevante poiché lo studio al M.E. delle biopsie renali permette non solo di definire la diagnosi delle differenti nefropatie, ma anche di otte-

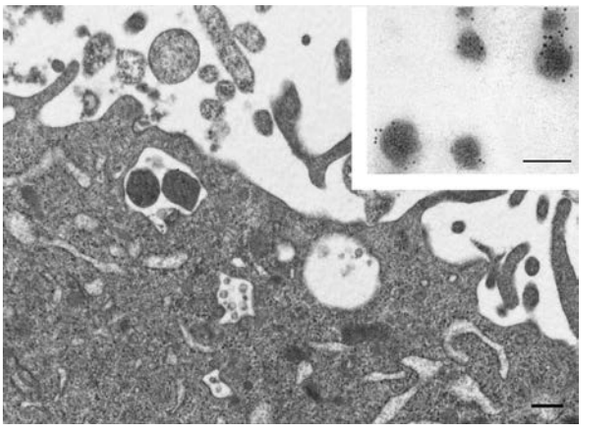


Figura 2. Particolare dell'ultrastruttura di una cellula di melanoma umana in cultura. Nell'inserto microvescicole (esosomi) rilasciate dalle stesse cellule tumorali e immunomarcate con oro colloidale al fine di caratterizzarle localizzando proteine specifiche di membrana. Barra d'ingrandimento: 300 nm, inserto 100 nm.

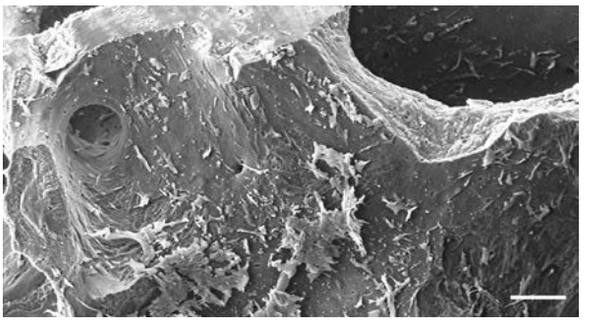


Figura 3. Cellule staminali mesenchimali umane coltivate su scaffold in idrossiapatite osservate in microscopia elettronica a scansione. L'immagine a basso ingrandimento permette di intuire la struttura dello scaffold "riassorbibile" che riproduce quella dell'osso. Barra d'ingrandimento: 150 μm.

nere una valutazione morfologica sullo stato di attività o di quiescenza delle malattie in atto (Figura 5).

Un'altra caratteristica del Consorzio, prevista dallo Statuto, è quella di avere finalità culturali e sociali tendenti a far conoscere la microscopia e promuovere il territorio che lo ospita, tramite iniziative culturali/scientifiche, anche a carattere divulgativo.

In questo quadro si inserisce il "Progetto Scuola Consorzio M.I.A.", nato con l'obiettivo di avvicinare gli studenti alla microscopia ed in generale al mondo della Scienza.

Questo progetto, promosso in collaborazione

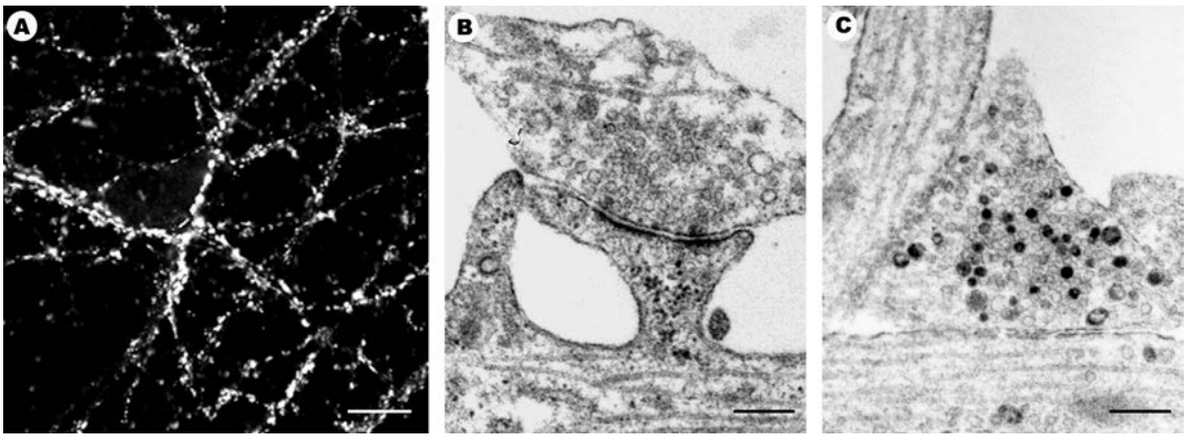


Figura 4. Sinapsi in neuroni in cultura osservate con diverse tecniche morfologiche. A) Microscopia confocale: immunolocalizzazione di una proteina vescicolare. B e C) Microscopia elettronica a trasmissione di sezioni ultrasottili di tessuto incluso in resina epossidica. In C è stata utilizzata la perossidasi per evidenziare le vescicole che, durante l'esperimento, sono entrate in contatto con l'ambiente extracellulare a causa di un ciclo di eso-endocitosi. Barra d'ingrandimento: A) 10 μm B,C) 300 nm.

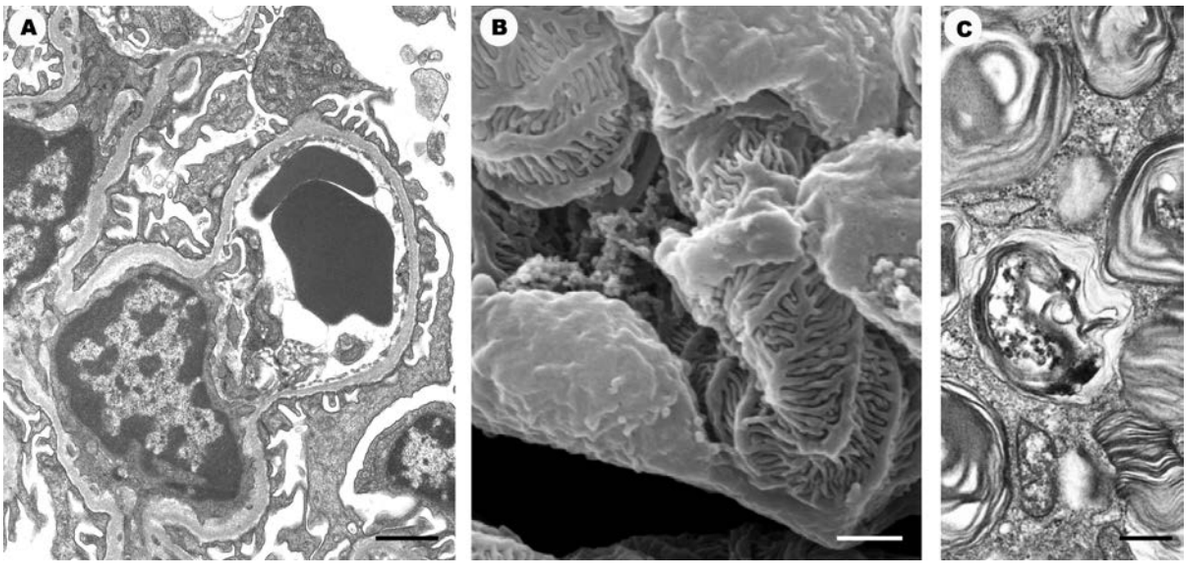


Figura 5. Microscopia elettronica a trasmissione di sezioni ultrasottili di tessuto incluso in resina epossidica **(A, C)** e microscopia elettronica a scansione (B) di glomeruli renali. In C: accumuli di materiale glicosfingolipidico osmiofilo (Zebra-bodies) all'interno dei podociti glomerulari, caratteristici della malattia di Anderson-Fabry. Barra d'ingrandimento: A,B) 1,5 μm C) 0,5 μm.

con l'Università di Milano-Bicocca, intende rispondere anche a precise indicazioni ministeriali tendenti ad arginare il rilevante e preoccupante calo del numero d'iscritti alle Facoltà scientifiche delle Università italiane negli ultimi anni, causato dal sempre minor interesse che i giovani rivolgono alle materie scientifiche.

Il Progetto prevede diverse iniziative rivolte a docenti e a studenti delle scuole di ogni ordine e grado. Sono previste lezioni teoriche e/o pratiche, anche presso le scuole, per approfondire temi che, secondo le esigenze didattiche, possono affrontare aspetti di biologia cellulare od aspetti, più tecnici, legati all'uso ed alle caratteristiche dei microscopi, nonché al loro utilizzo nel campo della ricerca e della diagnostica.

Sono previste visite guidate ai laboratori del Consorzio M.I.A. e "stages" per un numero limitato di studenti, selezionati in base alle attitudini e agli interessi. Questo progetto, partito un paio di anni fa, sta riscontrando un buon successo con un numero sempre crescente di richieste.

Fra le iniziative del Progetto Scuola s'inseriscono quelle di "Alla ricerca di forme e significati", sottoprogetto promosso in stretta collaborazione con l'Università di Milano Bicocca ed alcuni insegnanti di Scienze, Filosofia ed Arte di scuole di diverso orientamento (nella fase preliminare un Liceo Scientifico Tecnologico, un Liceo Artistico ed un Liceo Classico) del territorio della Brianza. Questo sottoprogetto verte sull'immagine microscopica, la complessità della sua analisi ed interpretazione e le analogie che queste immagini hanno con opere artistiche. In pratica si vuole sottolineare l'importanza di affrontare un argomento da molteplici punti di vista. Lo scopo è di dimostrare che valorizzando e integrando conoscenze, capacità e competenze diverse è possibile ottenere validi risultati in campo scientifico, artistico ma anche sociale, favorendo l'inserimento di ogni singolo individuo.

Gli obiettivi previsti sono:

- stimolare le potenzialità di ciascuno ragazzo attraverso un approccio multidisciplinare che permetta di scegliere gli aspetti che più interessano, valorizzarne e svilupparne le differenti competenze (pratiche o teoriche), evidenziandone le reciproche implicazioni;
- favorire l'integrazione, sviluppando l'attitudine alla collaborazione;
- educare i giovani ad affrontare i problemi da punti di vista diversi, con approcci metodologici, linguaggi differenti e fornire agli studenti utili stimoli all'orientamento scolastico e professionale.

"Alla ricerca di forme e significati" prevede oltre al lavoro di gruppo portato avanti nelle singole scuole, iniziative pubbliche tra cui una serie di Seminari didattici tenuti da esperti di vari settori a supporto delle attività del Progetto ed un ciclo di Incontri pubblici, dal titolo "Punti di vista - Alla ricerca della realtà" con personalità autorevoli, quali Don Virginio Colmegna, Giulio Giorello, Jacopo Meldolesi, Valerio Onida, Edoardo Rosati.

Il Progetto ha già ottenuto, fra gli altri, il patrocinio dell'Agenzia del MIUR per lo Sviluppo dell'Autonomia Scolastica e della Provincia di Milano oltre al sostegno della Fondazione della Comunità di Monza e Brianza, della Fondazione internazionale "Invest for Children Foundation" e d'importanti enti e aziende.

La speranza è però quella di riuscire ad allargare il Progetto coinvolgendo anche scuole al di fuori del territorio che ci circonda. Il fatto che del progetto si sia recentemente occupata, con un lungo articolo, una rivista molto diffusa fra i docenti delle scuole a livello nazionale è una buona partenza.

Un'altra iniziativa prevista da "Alla ricerca di forme e significati" è un Concorso artistico di rielaborazione delle immagini prodotte al microscopio, aperto agli studenti delle scuole superiori e ai giovani artisti. Il bando, che sarà pubblicato nei prossimi mesi, prevede che gli artisti prendano spunto per le loro opere da immagini ottenute con microscopi di diverso tipo. Queste immagini saranno scelte fra quelle ottenute dagli stessi studenti durante le prime fasi del progetto, tra quelle prodotte dal Consorzio M.I.A. ma anche fra quelle proposte dai vari ricercatori che si occupano di microscopia, ad esempio anche dai lettori di questo articolo che desiderino aderire all'iniziativa. Chiunque sia interessato può contattare il Consorzio M.I.A. all'indirizzo: *info@consorziomia.org*.

Certamente il percorso per realizzare pienamente quanto previsto dallo Statuto del Consorzio è ancora da completare. La speranza è di riuscire a crescere trovando sempre gli stimoli necessari nelle richieste che perverranno, magari anche da parte vostra. Decisive per l'attuazione degli obiettivi del Consorzio saranno però le possibilità d'investimento da parte dei Soci, attuali e futuri.

Si riporta di seguito una selezione delle pubblicazioni del Consorzio M.I.A..

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Cell death in human articular chondrocytes: an ultrastructural study in micromass model

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Summary

Chondrocyte apoptosis is known to contribute to articular cartilage damage in osteoarthritis (OA) and is correlated to a number of cartilage disorders. Micromass cultures represent a convenient means for studying chondrocyte biology, and, in particular, their death. In this study, we present the first ultrastructural analysis on chondrocyte death experimentally induced by different agents, all known to be powerful apoptotic triggers.

Chondrocytes were obtained from subjects undergoing joint arthroplasty. At the end of the maturation, they were treated as follows: 10 or 30 μM etoposide for 24h, UV-B for 30 min followed by 4h recovery, 200 or 500 nM staurosporine for 24h, hyperthermia for 1h at 43°C followed by 4h recovery. They were processed for TEM and immunofluorescence.

Control chondrocyte morphology appears similar to that of human articular cartilage. Proteoglycans and collagen fibers are present in the intercellular space, indicating a good extracellular matrix (ECM) production. Etoposide, when effective, induces necrosis. UV-B treated cells show chromatin condensation and pore clustering, typical of apoptotic nuclei. Hyperthermia seems to induce apoptosis in the presence of abundant ECM, giving, differently, a general necrosis when ECM is scarse. Staurosporine has no effect at 200 nM concentration, but frequently, at 500 nM, chromatin condensation appears. Chromatin clumping appears different from that of classical apoptotic models: Roach *et al.* proposed the term "chondroptosis" to indicate this type of cell death. Cells appear shrunk and the nucleus contains condensed chromatin, not marginated into large solid masses, but in small patches, mainly at nuclear periphery. Chondrocytes seem so to undergo apoptosis in a peculiar typical manner.

Keywords: micromass, chondrocyte, apoptosis, osteoarthritis.

Introduction

Osteoarthritis (OA) is a slow progression degenerative disorder, characterized by pain, stiffness and joint functional limitation. It is the most common rheumatic disease with the highest economic impact (Attur *et al.*, 2002), generally affecting both sexes: before 45 years it mainly affects men, while it is more frequent in woman after 45 years. The risk factors, of this pathology are obesity, smoke as well as metabolic, mechanical and genetic factors.

The inflammatory factors activate chondrocytes, the unique cell component in articular cartilage, which are then no longer able to maintain tissue homeostasis. They undergo a number of cell reaction patterns including hypertrophy and terminal differentiation, as it occurs in the hypertrophic zone of the growth plate (Sandell and Aigner, 2001). A crucial role in OA pathogenesis is played by the extracellular matrix (ECM), which seems to loose its remodelling properties, thereby contributing to chondrocyte apoptosis (Kim and Blanco, 2007; Del Carlo and Loeser, 2008).

This type of cell death is known to contribute to articular cartilage damage in OA (Aigner *et al.*, 2001; Olivotto *et al.*, 2007; Scher *et al.*, 2007; Johnson *et al.*, 2008) and is correlated to a number of cartilage disorders. Roach proposed the term *chondroptosis* to evidence the fact that such cells undergo apoptosis in a non-classical manner that

appears to be typical of chondrocyte programmed death *in vivo* (Roach *et al.*, 2004). Nevertheless, its study *in vitro* has been long hampered by the difficulty to reproduce the *in vivo* cell conditions. Human chondrocyte primary monolayer culture does not recover a proper microenvironment comparable with *in vivo* ECM, and so it cannot be considered a reliable experimental model (Kavalkovich *et al.*, 2002). Differently, micromass cultures represent a convenient means for studying chondrocyte biology, pathology and death. In particular, they can be considered a useful experimental model to investigate cartilage response to physical or chemical agents (Kafienah *et al.*, 2007). In this study, we present the first morpho-functional analysis on human chondrocyte death experimentally induced by a number of agents, all known, in most common cell systems, to be powerful apoptotic triggers.

Materials and Methods

Chondrocyte cultures

Articular cartilage tissue specimens were withdrawn from the tibial plateau of OA patients undergoing joint arthroplasty. Samples were processed with a sequential enzymatic digestion (12). Chondrocytes (500,000), at first passage (p1), were pelleted (by centrifugation for 20 min, at 4°C, at 740 g) in Sarstedt cryotubes (Numbrecht, Germany) and then differentiated in 10% serum medium in standard oxygen pressure, in the presence of 50 µg/mL ascorbic acid, with medium change every second day. Immediately after centrifugation, the cells appeared as a flattened pellet at the bottom of the tube. One day later, the pellet had a thickened lip and, in a week, it became spherical without any increase in size. In 2-3 weeks, it changed from white and opaque to a glistening transparent structure (Zhang *et al.*, 2004; Olivotto *et al.*, 2008).

At the end of the maturation, chondrocyte micromasses were treated as follows:

- UV-B (312 nm) for 30 min, followed by 4h recovery;
- 200 or 500 nM staurosporine for 24h;
- hyperthermia for 1h at 43°C, followed by 2 or 4h recovery;
- 10 or 30 µM etoposide for 24h;
- 0.3 or 0.5 mM H_2O_2 for 1h;
- 60 or 90 µM cisplatin for 24h.

SEM

After washing, control micromasses, were fixed with 2.5% glutaraldehyde in 0.1 M cacodylate buffer for 3 h. They were quickly washed and post-fixed with 1% OsO_4 in the same buffer for 1h. A progressive alcohol dehydration was performed, followed by specimen critical point drying. After mounting on conventional SEM stubs by means of silver glue, specimens were gold-sputtered (Battistelli *et al.*, 2005). Observations were carried out with a Philips 515 scanning electron microscope.

TEM

Control and treated chondrocyte micromasses were fixed with 2.5% glutaraldehyde in 0.1 M cacodylate buffer for 3 h, post fixed with 1% OsO_4 in the same buffer for 1 h, alcohol dehydrated, and embedded in araldite, as previously reported (Luchetti *et al.*, 2006). Thin sections were collected on 400 mesh nickel grids and stained with uranyl acetate and lead citrate (Battistelli *et al.*, 2005). The observations were carried out with a Philips CM 10 electron microscope at 80 kV.

Immunofluorescence

IF staining of the main ECM components (aggrecan, chondroitin-4-sulphate and chondroitin-6-sulphate, collagen type II and type I) was performed, to assess the chondrocyte differentiation degree. Five micrometers sections of OCT embedded, snap frozen (liquid nitrogen) micromasses were fixed with 4% paraformaldehyde in PBS for 30 min. After antigen unmasking for 30 min at 37°C with 2 mg/mL hyaluronidase (required for collagen type II and collagen type I) or with 0.02 U/mL ABC chondroitinase (required for chondroitin-6-sulfate, chondroitin-4-sulfate, and aggrecan), a step to block nonspecific binding was performed with 2% BSA, 0.1% Triton, and 5% normal goat serum in TBS for 45 min at room temperature. Next, a panel of mouse monoclonal antibodies (Chemicon International, Temecula, CA), including antibodies to the different components of the branch- shaped complex named aggrecan (core protein and sulphated GAG), was applied (Battistelli *et al.*, 2005). Then, the slides were mounted with antifading (1,4-diazabicyclo octane; Sigma, St Louis, MO) and analyzed with a Nikon Eclipse E 600 fluorescence microscope. Sulphated GAG may immobilize soluble factors bearing heparin-binding domain, such as chemokines.

Results

SEM shows inner and outer micromass features: on the surface cells appear closed one another (Figure 1 A, B) while inner structure reveals wide spaces containing ECM (Figure 1 A, C).

Chondrocyte morphology in control condition appears very similar to that of human articular cartilage (Figure 1 D, E). Cells are rounding or slightly elongated with plurilobated nucleus and diffusely dispersed chromatin. The nucleus frequently, appears eccentrically located, due to a relevant amount of lipid vacuoles., We can often observe large amount of glycogen masses and iso-

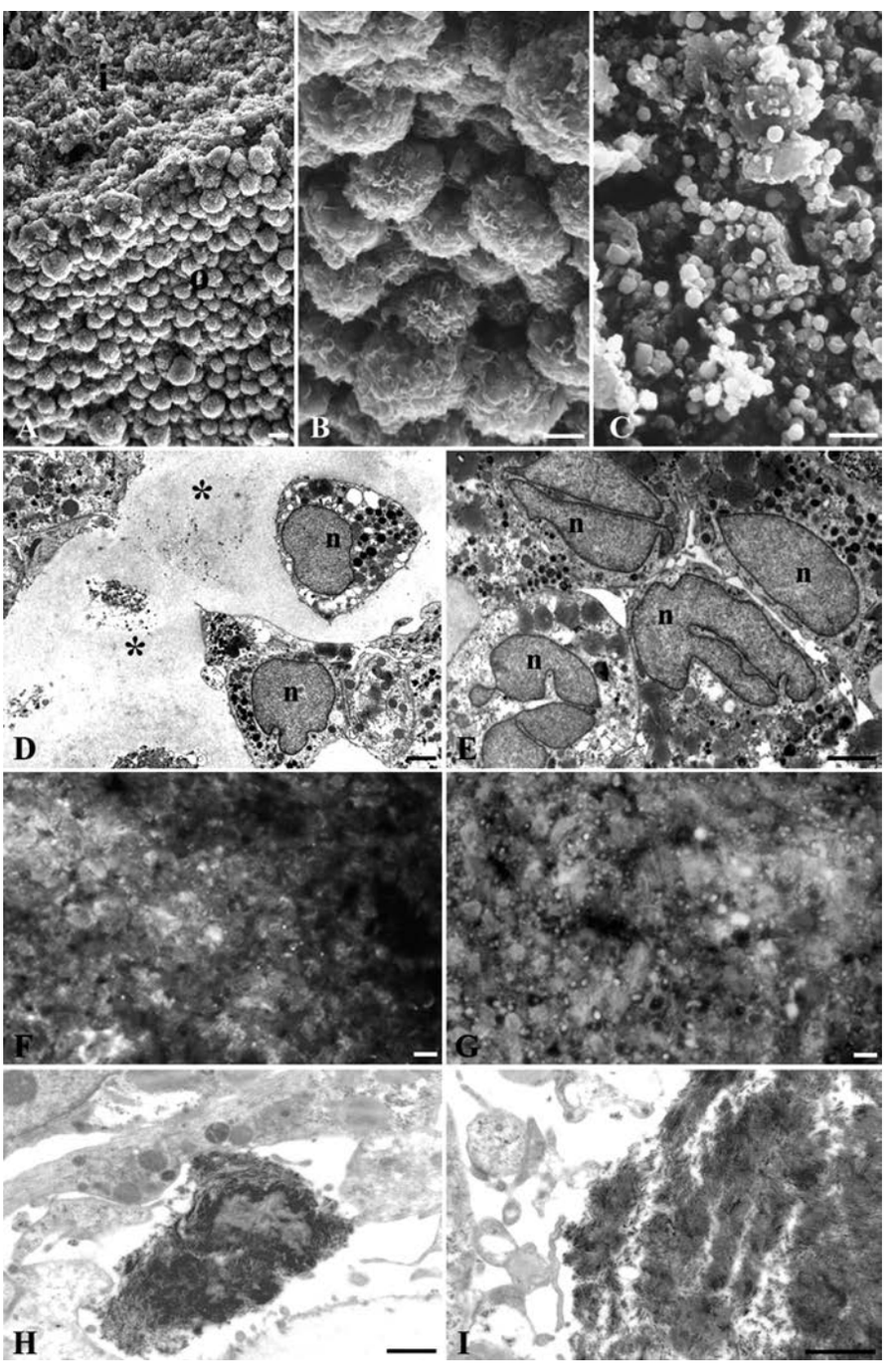

Figure 1. SEM (A, B, C), TEM (D, E, H, I) and IF (F, G) of control micromasses. SEM shows inner (A, i) and outer (A, o) micromass cells, better shown in B and C, respectively. TEM observation shows ECM (*) and nuclei (n) with diffuse chromatin (D, E). At IF staining, proteoglycan (F) and collagen (G) presence appears. In H and I calcification areas appear in the intercellular spaces. A, bar = 0,1 µm; B, C, bar = 5 µm; D, E, F, G, H, I, bar = 1 µm.

lated granules scattered throughout the cytoplasm. Proteoglycans and collagen fibers are present in the intercellular space, indicating a good ECM production (Figure 1 F, G). Occasionally it is possible to observe an initial periodic collagen organization, although less recognizable than that of mature collagen (*not shown*). Sometimes calcification areas appear (Figure 1 H, I).

UV-B, a frequently utilized apoptotic trigger, but with a partially unknown mechanism of action, induces chromatin condensation and pore clustering, typical features of apoptotic nuclei (Figure 2 A, B). Occasionally, a characteristic swelling - suggestive of necrotic progression - can be revealed

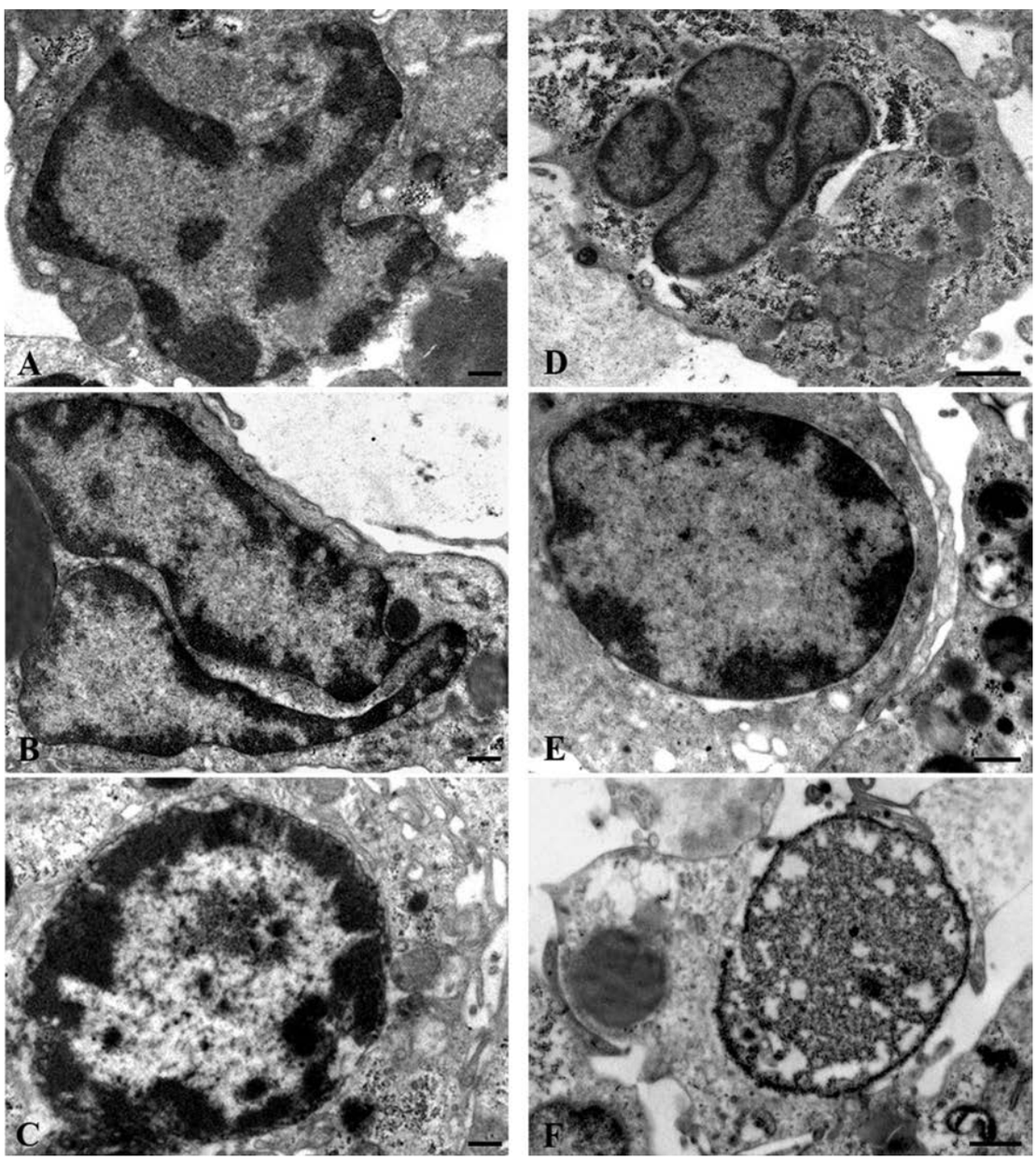

Figure 2. Chondrocytes after UV-B (A, B, C) and staurosporine (D, E, F) treatment. UV-B induces chromatin condensation and nuclear pore clustering (A, B). Occasio-nally inititial necrotic effects can be revealed (C). 200 nM staurosporine has no effect (D), but 500nM induces chromatin condensation (E) and sometimes, necrosis (F). A, B, C, D, E, F, bar = 1 µm.

(Figure 2 C). Staurosporine, a PKC inhibitor, has no effect at 200 nM concentration (Figure 2 D), but frequently, at 500 nM, chromatin condensation (Figure 2 E) and a certain necrotic effect (Figure 2 F) appear.

Hyperthermia, generally considered a powerful apoptotic trigger, induces nuclear modifications suggestive of chondroptosis after 2h post-incubation (Figure 3 A, B, C). Moreover, after 4h post-incubation, it seems to induce apoptosis in the presence of abundant ECM (Figure 3 D, E), showing, differently, a general necrosis when ECM is

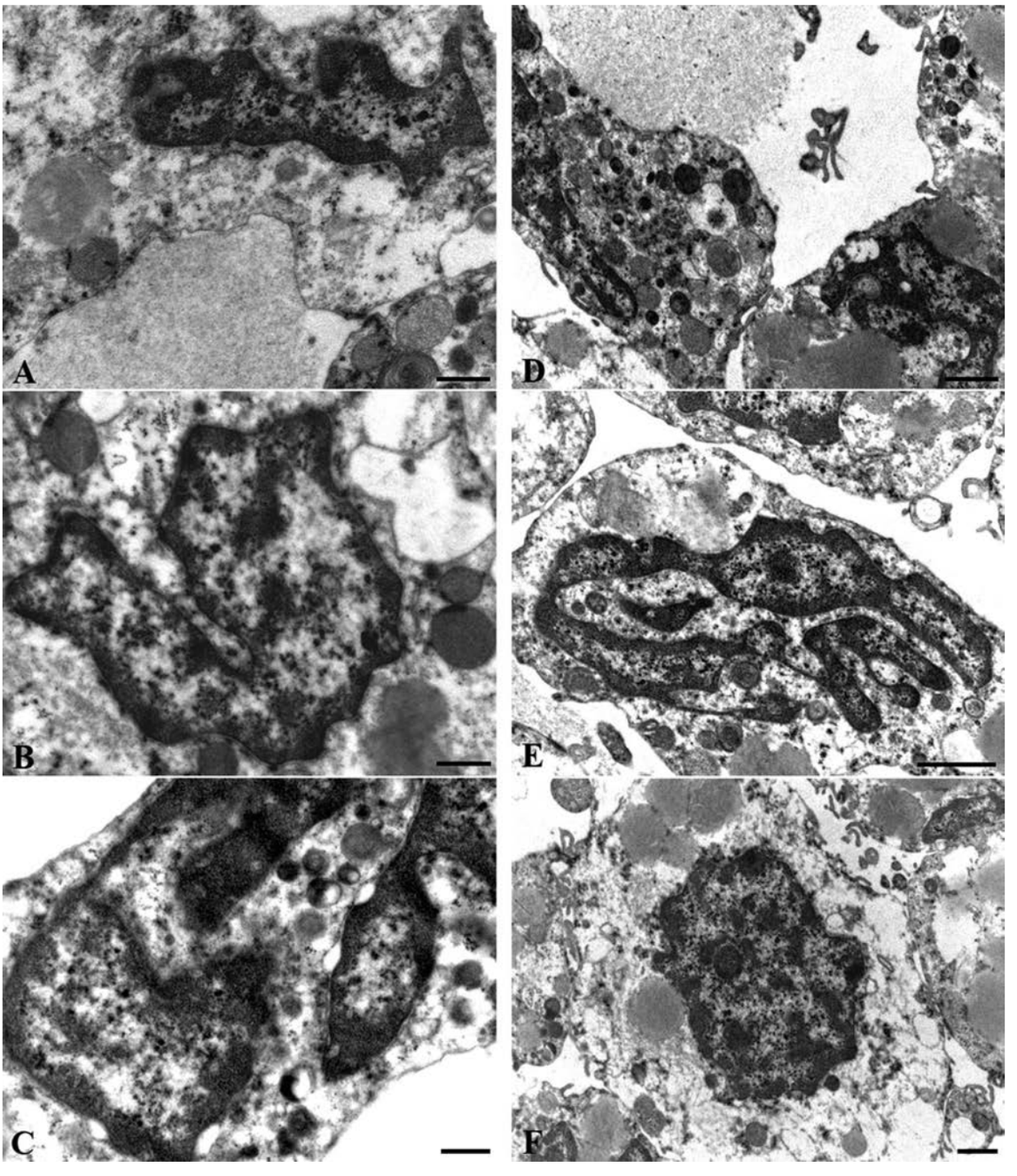

Figure 3. Hyperthermia induces nuclear changes suggestive of chondroptosis after 2h post-incubation (A, B, C). After 4h post-incubation, hyperthermia causes apoptosis in the presence of abundant ECM (D, E), and a general necrosis when ECM is scarce (F). A, B, C, D, E, F, bar = 1 μm.

scarce (Figure 3 F).

Etoposide, a topoisomerase I inhibitor, is poorly effective (Figure 4 A, C, D), occasionally inducing necrosis (Figure 4 B).

H_2O_2 and cisplatin, have not effect at low concentration but, at high ones, they induce a weak apoptotic response (*not shown*).

Therefore, chondrocytes show a heterogeneous behaviour in response to different treatments, and dependently on cartilage micromass conditions.

Extracellular matrix seems to influence chondrocyte response, being micromasses with abundant ECM more resistant to the damage, and directed to apoptotic rather that to necrotic death.

Moreover, the extent of ECM does not seem to decrease during treatments.

In all conditions in which we observed chromatin condensation, it appears different from that of classical apoptotic models. Roach *et al.* (Roach and Clarke, 2000) proposed the term "chondroptosis" to indicate this type of cell death, which was observed in the majority of articular hypertrophic chondrocytes *in vivo* (Blanco *et al.*, 1998).

In our experimental system chondrocytes seem to undergo apoptosis in a non-classical manner, but in a way that seems typical for them, which can be correlated to chondroptosis. As in commonly reported apoptosis, cells appear shrunk and the nucleus contains clumped chromatin. However, the chromatin is not marginated into large dense masses, mostly cup-shaped, but in small patches, mainly located at nuclear periphery (Figure 5 A, B, C, D, E). Chondroptosis involves an initial increase in the endoplasmic reticulum and Golgi apparatus, reflecting an increase in protein synthesis.

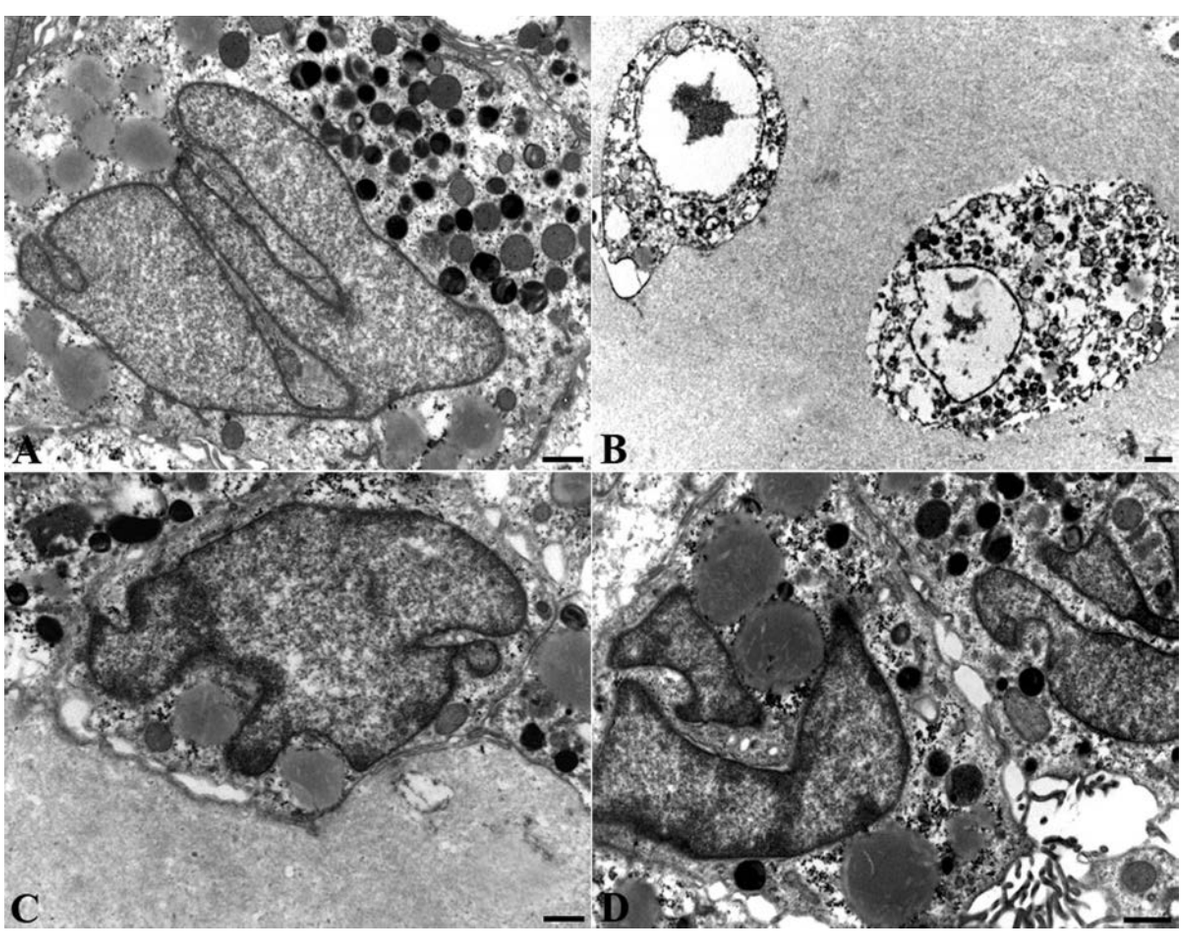

Figure 4. Necrosis, occasionally appears in etoposide-treated specimens (B), even if the trigger has generally an irrelevant effect (A, C, D). A, B, C, D, bar = 1 µm.

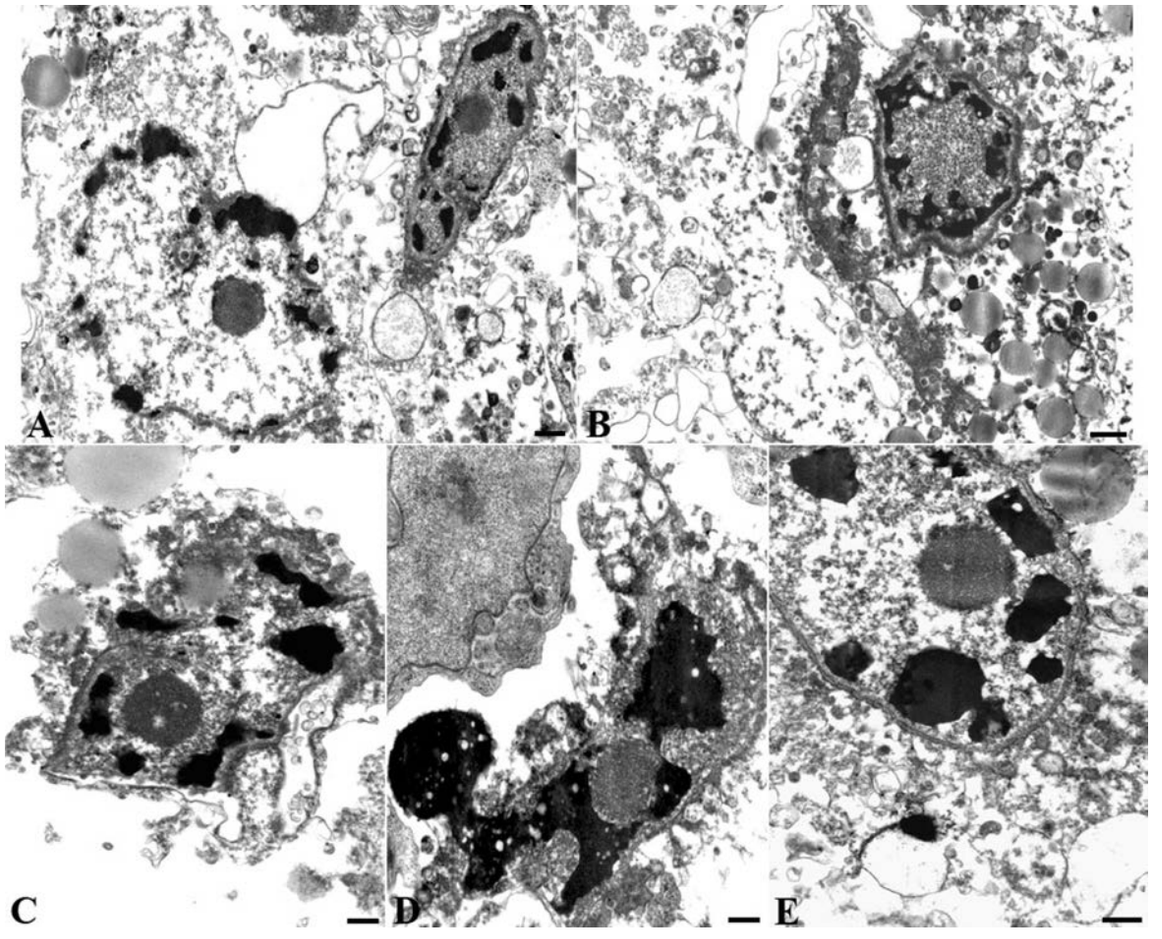

Figure 5. General ultrastructural features of chondroptosis. A, B, C, D, E, bar = 1 μm.

Table 1.

	Apoptosis	*Condroptosis*	*Necrosis*	*ECM*
Control	-	-	-	+
UV-B (312 nm)	+	+	-	+
500 nm Staurosporine	+-	+	+	+
Hyperthemia 2h post-incubation	-	++	+	+
Hyperthemia 4h post-incubation	-	++	++	+
10 μm Etoposide	-	-	-	+
30 μm Etoposide	-	-	+	+
0.3 or 0.5 mM H_2O_2	-	-	+	+
60 or 90 μM Cisplatin	-	-	-	+

Conclusion

Our observations, summarized in Table 1, demonstrate that:

- human articular chondrocytes appear able to undergo apoptosis after UV-B treatment;
- staurosporine and hyperthermia apparently induce chondroptosis;
- hyperthermia effect seems to depend on ECM quantity:
- etoposide is mostly a necrotic trigger.

Chondrocytes cultured in the tridimensional micromass model seem to evidence variable responses, when stimulated by apoptotic triggers. If compared to the classical and more widely described monolayer culturemodel, they present the peculiar characteristic to live in close contact with an ECM microenvironment, which, evidently, regulates also their reaction to external stimuli. Apoptotic/necrotic/chondroptotic responses, shown by micromass chondrocytes, represent howewer, the expression of their death *in vitro*, which can be considered an important model to understand mechanisms underlying articular cartilage disorders.

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Quantitative evaluation of strain effects in STEM HAADF contrast

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Summary
In the context of the methodological studies aimed to give a quantitative evaluation of composition basing on High Angle Annular Dark Field (HAADF) STEM imaging, I propose to afford quantitatively the effect of a strain field varying along the electron propagation direction. I propose, as a case study, the well known surface strain relaxation in a STEM specimen comprising an InGaAs-GaAs Quantum Well. I will demonstrate, by means of experiments and simulation that, surface strain relaxation produce characteristic intensity dips at the sides of the QW not ascribable to chemical effects. The origin of this contrast will be correlated with the characteristic phenomenon of channelling in zone axis conditions.

Keywords: HAADF, surface strain relaxation, channeling.

Introduction

The methodological research aimed to produce quantitative analysis based on high-resolution transmission electron microscopy (HRTEM) has reached, under many aspects, a good degree of maturity as many effects concurring to the image formation have been clarified (Coene *et al.*, 1992; Van Dyck and Op de Beeck, 1996; Kret *et al.*, 2001). On the contrary, in many cases, the use Scanning Transmission Electron Microscopy (STEM) technique with High Angle Annular Dark Field (HAADF) detector mainly remains qualitative as new methods to give a quantitative interpretation of HAADF images are still being developed (Anderson *et al.*, 1997; Liu *et al.*, 1999; Carlino and Grillo, 2005; Grillo and Carlino, 2008; LeBeau *et al.*, 2008). One of the main advantages of the technique is indeed its capacity to make evident a compositional variation through a change of the intensity. This is particularly appealing in the case of imaging in low index zone axis conditions for which the chemical information on a single atomic column can be readily obtained.

The strong compositional sensitivity is also related to the use of a large collection angle. Indeed for a sufficiently large scattering angle the scattering contribution is dominated, at room temperature, by the thermal diffuse scattering (TDS). One of the peculiarities of this scattering mechanism (but also of the elastic contribution at high angle (Rafferty *et al.*, 2001)) is that the scattering contributions of atoms sum incoherently with each other (Pennycook and Jesson, 2001). This is quite different from what happens with HRTEM images where the interference of the coherent scattering from each atom needs to be considered. This highly coherent nature of the HRTEM image formation makes it intrinsically more sensible to any non-periodic effect of the crystalline structure and in particular to the strain fields. Such effects superimpose and often dominate on compositional effects (Ruvinov *et al.*, 1995; De Caro *et al.*, 1997). It results therefore evident the advantage of an incoherent technique as HAADF for its possibility to reduce strain related effects. Experimentally it is indeed observed a drastic reduction of such effects when the detector inner aperture is increased (Hillyard and

Silcox, 1995; Yu *et al.*, 2004).

For sufficiently high inner angle of the detector the simplest approach for interpreting HAADF imaging assumes the intensity to be the convolution of a function representing the probe at the entrance of the specimen and a function accounting for the scattering by the atomic columns (Anderson *et al.*, 1997). In practice this is equivalent to assume that a TDS wave is produced at each atomic position with intensity proportional to the intensity of the impinging beam at that position. The success of this assumption is, in most cases, relatively good. This makes the HAADF imaging in zone axis conditions a valid instrument for the analysis of the atomic positions in complex structures (interfaces defects and so on) (Xin *et al.*, 1998; Lopatin *et al.*, 2002; Klenov *et al.*, 2005). In spite of this success this simplified scheme may be inadequate for the prediction of finer effects in the HAADF contrast, starting from the intensity dependence on thickness, the effect of static displacement (this has been already considered in a previous article (Grillo and Carlino., 2008)) or of strain that will be the object of this work. In particular these effects show up most importantly right in the low order zone axis conditions where the technique shows most of its advantages. It is worth mentioning that these fine effects cannot be completely eliminated even with the use of a large angle. Their evaluation becomes therefore necessary whenever accurate quantitative chemical information need to be extracted from the HAADF images. In these cases the use of simulations becomes mandatory for a correct image interpretation and quantification.

It is, at this point, interesting to briefly discuss the origin of the deviations from the simple image interpretation. Interestingly the incoherent nature of the TDS waves remains valid to a very good degree of approximation. Conversely the most important pitfall of the simple convolution model is that it does not take into account the interaction of the electron beam with the sample. Specifically in the case of zone axis conditions a narrow probe excites predominantly the columnar Bloch states (also named 1s) and several less localized stated (Anderson *et al.*, 1997). The large excitation of the 1s states is also referred to as channelling. The actual wavefunction inside the sample is the result of the interference of all these Bloch states. The first evidence of this phenomenon is visible for example in the oscillation of the derivative of the intensity with specimen thickness (Voyles *et al.*, 2003).

A more indirect evidence of this arises from the calculation and observation of the dependence on mistilt of the HAADF intensity. Small tilts off the zone axis condition have the effect to reduce the average HAADF intensity in a unit cell while leaving the atomic fringe pattern almost unchanged (Maccagnano-Zacher *et al.*, 2008). This reduction becomes even more evident when passing from crystalline to amorphous materials (Yu *et al.*, 2008). These evidences have convincingly demonstrated that the preferential propagation of electrons along highly symmetric directions strongly affects the HAADF average intensity. As a consequence of these observations it can be predicted that any perturbation of the columnar order and in particular strain effects can produce contrast in HAADF images. While these effects are often neglected in literature, in a few significant cases evidences for strain related contrast in HAADF have been shown (Treacy *et al.*, 1985; Cowley and Huang, 1992; Perovic *et al.*, 1993; Amali *et al.*, 1997; Liu *et al.*, 2001; Fitting *et al.*, 2006).

Two kinds of mechanisms have been claimed to be involved in the formation of the HAADF strain contrast. The first, sometimes referred to as Huang scattering, is related to the increase of the diffuse scattering at high angles as an effect of the increased static disorder. This mechanism has been claimed to be at the origin of the intensity increase of both high angle transmission electron microscopy and, to less extent, HAADF in proximity of dislocations (Wang 1994). The second mechanism is related to dechannelling, namely the reduction of the 1s contribution to the electron wavefunction due to interband scattering between Bloch waves, induced by local strain. Strain indeed produces a faster depletion of the states localized to the atomic columns in favour of less localised states (Cowley and Huang, 1992; Perovic *et al.*, 1993). Both mechanisms are certainly active in the case of a HAADF image of an extended defect with the interband scattering effects being dominant.

It must be stressed that also the static disorder is known to produce an interband scattering in the states excited by the probe. This has been used to explain the HAADF intensity reduction in presence of a random strain field on atomic scale (Yu *et al.*, 2004; Grillo and Carlino, 2008).

However, when extended defects are dealt with, the typical scale length of the strain field is larger and the mechanism of interband scattering is not merely the effect of local disorder: while slowly varying strain fields induce a shift of the electron wave-function with the atomic column the random displacement with its rapid oscillation along the propagation direction produces mainly a reduction of the 1s excitation (Plamann and Hytch, 1999).

In spite of this general wisdom about strain effects even tiny difference in the intensities are often interpreted directly as due to compositional effects. The main reason for this could possibly lie in the lack of a quantitative evaluation of the size of strain effects.

For this reason I will analyse the case study of strained InGaAs/GaAs quantum wells (QWs) for which the chemical variation between the well and the barrier is generally considered to be the sole active contrast mechanism. A more accurate interpretation should otherwise consider that the operation of sample thinning to achieve electron transparency has induced surface relaxation at the upper and lower specimen surface. This phenomenon is known to influence the TEM contrast and the produced strain field can be predicted with very good accuracy (Wang 1994; De Caro *et al.*, 1997). For this reason it represent an ideal benchmark to test strain effects in HAADF. It is the aim of this work to evaluate quantitatively by both simulations and experiments such effects. In a first part of this work the phenomenology of the HAADF contrast as a function of different experimental parameters is described and discussed to exclude other possible contrast mechanisms. In a second part the experimental contrast is compared with multislice simulations in order to verify the quantitative match of the contrast profiles.

Materials and Methods

A sample consisting of three pseudomorphic QWs of $In_xGa_{1-x}As$, with In content x=0.05, 0.12 and 0.24 was grown by molecular beam epitaxy on GaAs (001) (Rubini *et al.*, 2006). The In content in the QWs was larger for the QW closer to the surface. The specimens for STEM experiments have been prepared in <110> cross section geometry by mechanical grinding and ion milling, following a well established procedure (Grillo and Carlino, 2008). The relevant experiments have been performed with a JEOL 2010F equipped by field emission gun and objective lens with a measured spherical aberration coefficient Cs = (0.47±0.01) mm, capable of a resolution, in HAADF, of 0.126 nm. All HAADF images were acquired by using an illumination convergence angle of 14 mrad and a detector collection angle of $84<2\vartheta<224 mrad$. HAADF images in <110> zone axis were acquired for different STEM specimen thicknesses. The specimen thickness was measured by the projections methods and, where necessary, confirmed by convergent beam electron diffraction (Williams and Carter, 1996). Moreover the specimen tilt was also measured by stopping the beam on a selected position and acquiring by the CCD the relevant diffraction pattern. The calibration of the camera length of such pattern permits to directly extract the tilt angle from the distance between the centre of the transmitted beam circle and the centre of Laue zone.

Results

Figure 1 shows a typical low magnification HAADF image of the sample along with the relevant line profile. All line profiles in this work have been obtained by a lateral averaging in the direction orthogonal to the growth direction to reduce the statistical noise and the influence of surface artefacts. The vacuum on the side of the specimen is clearly visible and it can be used for an evaluation of the effective dark counts. The intensity levels have been here expanded in order to give evidence to the features inside the sample. The most prominent feature is the presence of the three QWs with decreasing In concentrations at increasing distances from the surface. The difference in the In composition in the different QWs is visible as a different contrast to the GaAs barriers. In particular the inner QW has the lower intensity since it contains less In. A linear interpolation for the GaAs level has been also indicated with a dashed line as guide for the eyes.

In these conditions Figure 1 reveals a reduction of the HAADF intensity at one side of the outermost QW (with x=0.24) and to a lower extent in the others. The size of the contrast due to these intensity dips is of the order of 20-30% of the QW contrast and is typically visible in the greyscale dynamic conditions used to appreciate

the QWs contrast.

The intensity drops below the average GaAs just at the side of the QW and then rises slowly until it reaches a flat value at more than 10 nm from the QW interface. This feature is particularly interesting because in a sample comprising only In,Ga and As (with no significant concentration of vacancies) no intensity level is expected below the GaAs level. It is also worth noting that the QW itself shows a relatively smooth profile at the interfaces.

I will concentrate on the origin of the intensity minimum in proximity of the interfaces of the QWs. To further characterize this effect a systematic variation of the imaging parameters has been performed. In particular we defined the contrast as:

$$C = \frac{I}{I_0}$$

I_0 is an intensity reference level obtained by linearly interpolating in the well region and its proximity the intensity profiles in the GaAs barriers. This procedure has been performed to eliminate the effects on the intensities given by the thickness increase moving toward the inner part of the sample.

A first series of experiments were performed by changing the specimen orientation by few mrad in order to evaluate whether these effects may be related to any miss-orientation of the specimen.

The intensity minimum at the interfaces varies in depth and position depending on the experimental conditions. By varying the angle of tilt the intensity minimum move from the left (refereed to Figure 1a) to the right interface of the QW. For the intermediate value at the exact zone axis conditions, less pronounced minima are found at both interfaces.

This behaviour is well shown by Figure 2 in which the contrast profiles obtained for different specimen tilt conditions are shown. The figure refers to the In rich QW and the measured specimen thickness is in this case 42±3 nm. For large tilt the intensity minimum on the right toward the specimen edge increases while on the other interface the minimum is substituted by an intensity peak. Moreover for 9 mrad tilt the intensity in the QW region is roughly 30% higher than in the zone axis conditions.

A second kind of experiment was performed by changing the specimen thickness: in this case the relative importance of the dip in the intensity increases for decreasing thickness while it disappears almost completely for very thick samples (100 nm). Figure 3 shows the intensity contrast at the intensity minimum at exact zone axis conditions as a function of the specimen thick-

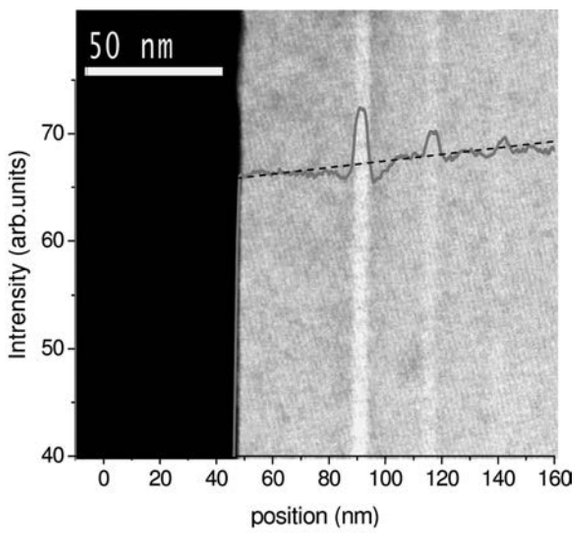

Figure 1. Low magnification HAADF cross sectional image of the sample in the InGaAs QWs region.

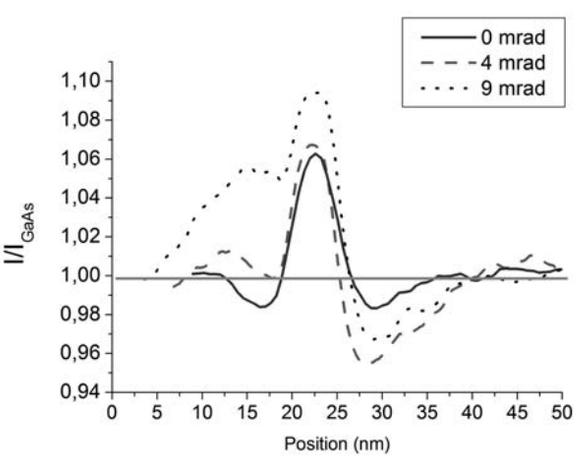

Figure 2. HAADF Intensity profiles of the sample for three different specimen tilt conditions in the QW with 24% In.

ness. A clear trend is visible confirming the reduction of the dip for increasing thickness. A fit with a ratonal function has been also added as a guide for the eyes. Summarizing, the experiments have produced the following evidences about the nature of the dip at the side of the QW.

1) The contrast of the intensity minima at the two interfaces can be varied by varying the tilt. In the cases of larger tilt one of the two minima can disappear while the other is strongly enhanced.
2) The contrast depth at the minimum decreases as the specimen thickness increases.

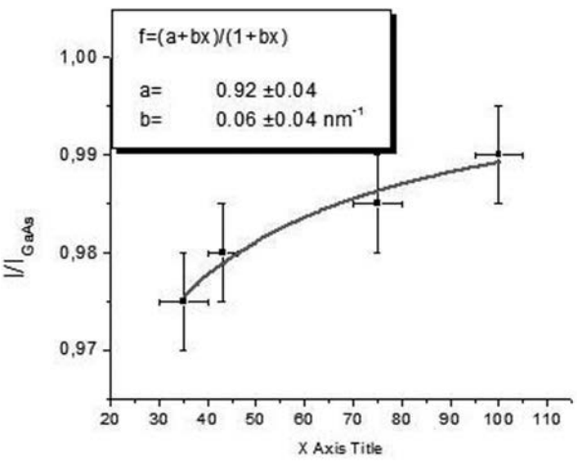

Figure 3. Plot of the Intensity at dip at the side of the QW normalized to GaAs level as a function of the specimen thickness. A plot with a rational function is also indicated.

Discussion

I have considered different contrast mechanism to explain the aforementioned evidences. The first is the presence of a large amount of point defects and composition anomalies at the interfaces of the QW. Yu at al (Yu *et al.*, 2004) have already shown that Si implanted by ion bombardment can show a drastic reduction of its HAADF intensity. According to their work this reduction is mainly ascribable to a reduction of the channelling conditions. More in general this mechanism should be the dominant contrast mechanism at any point defect (Perovic *et al.*, 1993; Hillyard and Silcox, 1995).

The experimental results indicate however that the intensity variations at the InGaAs/GaAs interfaces cannot be ascribed to point defects. As a matter of facts, as the specimen undergoes a small misstilt outside the zone axis conditions the excitation of the columnar states and consequently the total HAADF intensity is reduced: however a point defect will not have any preferential direction and the effect of the tilt should be similar at both interfaces of the QW and for any tilt. It is then impossible to introduce any asymmetry in the intensity at the two interfaces of the QW, as actually observed, as a sole effect of tilting.

The strain relaxation induced by the thinning of the specimen is the simplest explanation of the experimental features.

An atomistic model for the relaxed structure is sketched in Figure 4. A section of the atomic structure comprising the QW and part of the barrier is represented. The x direction has been chosen in the growth direction of the structure and z along the electron propagation direction. The structure should be ideally continued along the

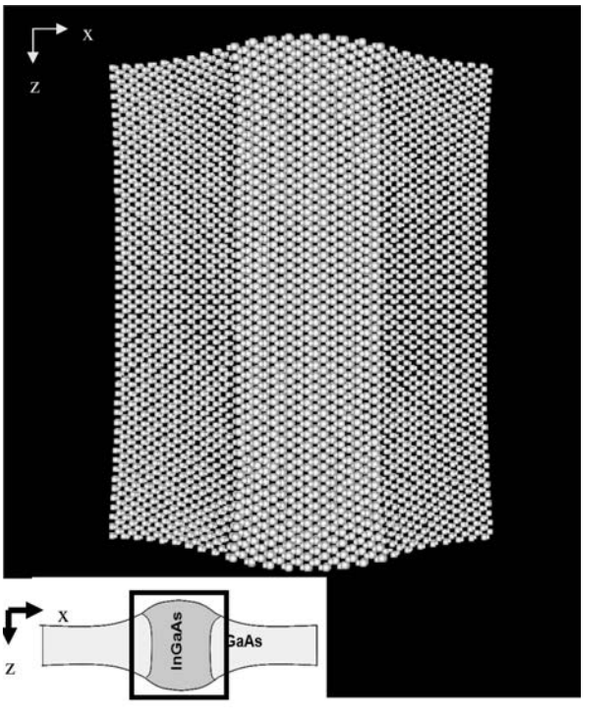

Figure 4. Atomistic model of the QW region with surface relaxation (Electron propagation direction is along z). The strain field has been enhanced by a factor 10 to provide a better visualization. A schematic of the Qw structure is also shown. The region of the atomistic model is indicated by a rectangle.

positive and negative x direction, while the upper and lower free surfaces in the z direction are clearly visible with their deformed contour: the deformation have been enhanced by a factor 10 to provide a better visualization.

In order to understand this structure it is worth reminding that in pseudomorphic InGaAs/GaAs QWs grown on GaAs substrates, the difference between the lattice parameters of the two materials is accommodated by tetragonal deformation of the InGaAs lattice. In a thinned (S)TEM specimen, the free surfaces orthogonal to the electron propagation direction permit a relaxation of the strain at the InGaAs/GaAs interfaces. As a consequence of this relaxation both GaAs and InGaAs are largely bent in the zone of the interface closer to the free surfaces.

Since the HAADF intensity in zone axis condition is strongly enhanced by channeling, the bending at the first few nm of the sample surface with a consequent lower excitation of the 1s will produce an intensity dip in the zone of the interface. It is worth noting here that for sample thickness larger than 20-30 nm the bending of the exit (the lower one in Figure 4) free surface will not influence too much the overall intensity because the 1s state is typically largely absorbed within this distance.

A small tilt off the z.a. conditions can have the effect of partially compensating the effect at one interface of the QW while decreasing the excitation of columnar states on the other one, thus explaining evidence 1). Conversely when the sample thickness is increased, the relative weight of surface effects is reduced in agreement with evidence 2).

In order to give a quantitative account for this model by simulations, multislice calculations in the frozen phonon approximation (Kirkland, 1998) have been performed.

As a first step, the realistic strain model for the QW structure in presence of free surfaces has been calculated by means of the finite elements calculation [FEMLAB software (www.femlab.com)]. The strain has been taken into account to calculate the atomic positions in an $In_xGa_{1-x}As/GaAs$ QW with x=0.24. Simulations have been performed for the case of specimen thickness of 40 nm. The multislice calculations have been performed by means of STEM_CELL (Carlino and Grillo, 2007), a simulation package based on Kirkland routines (Kirkland, 1998) that permits to speed up the simulations by means of parallel computing. In order to facilitate the simulation the atomistic model (like the one sketched in Figure 4) has been divided in sections used as input for the multislice. For each section of the atomistic model, the intensity has been calculated over a single unit cell in proximity of the centre of the selected section in order to reduce the effect of incorrect boundary conditions (see also (Grillo and Carlino, 2008).

In order to ensure a correct sampling of the minimum spatial frequency, the samples has been taken about 3 x 3 nm (depending on the local lattice parameter).

Figure 5 shows a direct comparison of simulation and experiment for a specimen thickness of 42±3 nm for the experiment and 40 nm for the simulation. Both images regard exact zone axis conditions.

The intensity shows a pronounced dip in proximity of the QW interfaces, while it slowly recovers the intensity of the unstrained case at larger distances. This behaviour is in excellent agreement with the experiments and is a demonstration that strain causes the observed variation of the HAADF intensity. Finally, it is worth noting that according to simulations inside the InGaAs QW the intensity is not flat but decreases at increasing distances from the centre. Unfortunately in exper-

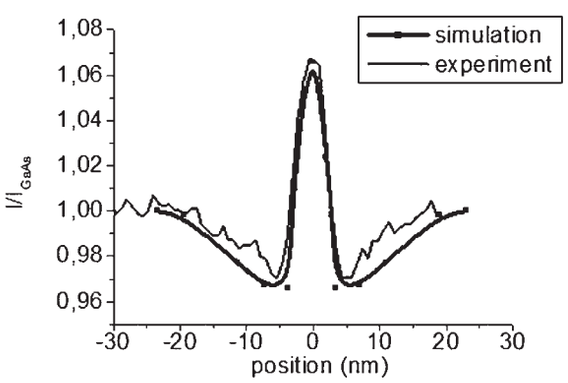

Figure 5. Simulated (solid line) and experimental (circles) intensity profiles for the 0.24% In QW. The specimen thickness is 40 nm for the simulation and 42±3 nm in the experiment. The simulation in dashed lines has been obtained scaling the intensity in the InGaAs layer for the Static Displacement correction as calculated in Grillo and Carlino (2008).

imental profiles this effect is completely superimposed to In segregation effects (Muraki *et al.*, 1992). Indeed experimental analysis of the lattice fringes distortion, performed on HRTEM images of the same sample, confirms that the In segregation accounts for the lineshape of the HAADF profile even without strain effects (Kret *et al.*, 2001). It is worth noting that the above considerations on strain effects can be extended to any other system where strain can be induced by the specimen thinning. The strain must be taken fully in account for a quantitative analysis of HAADF contrast experiments. It is further to be noticed that, because of the presence of strain, a sample tilt as small as 4 mrad can completely alter the intensity profile along the QW structure.

Conclusions

In this article the contrast in STEM -HAADF imaging produced by of a strain field varying along the electron propagation direction has been studied. The case study was the surface strain relaxation in a thinned specimen comprising InGaAs/GaAs QWs. The advantage of this structure is that the phenomenon has been widely studied by TEM analysis and the strain field can be predicted with good accuracy. It has been demonstrated by the relatively good agreement of experiments and accurate frozen phonon simulations that the main contribution of surface relaxation is to add one or two intensity dips, depending on the specimen tilt, in the barrier region at the sides of the QWs and an artificial smoothing of the QW intensity profile. Both effects should be accounted for when performing quantitative compositional analysis.

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