

European network on crystal polymorphism

an ESF Scientific Network

Polymorphism, which is the existence of more than one crystal structure of a substance, is of great theoretical and practical interest. The various crystalline forms of a polymorphic substance can have totally different physical, chemical or biological properties, sometimes with severe consequences across a range of industries from pharmaceuticals to foods. The existence of polymorphism has been known for 175 years, and while there have been many significant discoveries and research projects in the field, as yet there has been little concerted study of the fundamental phenomenon. Such a study would be of great theoretical interest, and also of practical benefit in a number of applied scientific fields involving chemical synthesis. This Network is creating a framework for such a co-ordinated study, to facilitate interdisciplinary research into polymorphism, and develop a European body of expertise in the theoretical methods, experimental techniques, and commercial exploitation.

Considerable research in polymorphism has been carried out, but often from an applied perspective in specific fields of application. This is because the practical consequences of polymorphism are wide variations in properties, and these have been of more immediate interest than the theory. The most dramatic and best known example carbon, which has several polymorphic forms, with graphite being soft and useful as a lubricant and writing material, while diamond is equally useful because of its hardness. There are many other more subtle examples with significant consequences within particular industries such as Glaxo-Wellcome's anti-ulcer drug Zantac, which has sold over \$30 billion to date and was subject to six years of patent litigation. This centred on polymorphism of the active ingredient ranitidine hydrochloride, which exists in two forms. The patent taken out by Glaxo-Wellcome on form I ran out in July 1997, but the company has a patent on a second form until 2004. Other firms wanted to enter the market by making the Form I after the July 1997 deadline expired, but it turned out that attempts to fabricate this led to the second form. Glaxo-Wellcome therefore argued that this would infringe the second patent.

Naturally such cases stimulate research into the relevant polymorphism, but there is a need now to consolidate all the different programmes and findings in the development of a more consistent approach. The Network is doing this by bringing together practitioners in many of the diverse fields where polymorphism is of relevance and interest, including crystallography, molecular modelling, thermodynamics, analytical chemistry, pharmacy, chemical engineering, materials science, and spectroscopy, plastic manufacture, and the paint industry. This list embraces a variety of pure and applied sciences as well as technology and manufacturing.

Among major scientific questions that the Network hopes to answer are whether it is possible to predict the existence of particular crystal structures from theoretical principles and if so determine what these principles are. Having accomplished this, the next goal would be to develop prescriptions for preparing these polymorphic structures whose existence has been proved theoretically. Thirdly, if it is possible to prepare these structures, it would be useful to be able to predict their properties in advance to determine whether they have practical application.

To achieve these difficult objectives it was necessary at the outset to identify those individuals with greatest expertise in the field from among the wide spectrum of relevant disciplines, including those cited above. This has already been achieved, and a solid core of expertise specific to polymorphism now exists. Many of the charter members of the proposed network now know each other, following the ESF-sponsored exploratory workshop in November 1999, at which virtually all of them were present. So while there had been a significant amount of informal networking before that ESF meeting, now many more people in the group are more aware of their potential for contributing to future polymorphism research. The aim now is to exploit this groundwork to fill the gaps in knowledge.

Europe is well placed to lead the world in filling these gaps. Polymorphism is one area in which Europe has more expertise than either Japan or North America. There is a clear opportunity to exploit that lead and build an ever-expanding community of closely co-ordinated academic and industrial practitioners.

The Network has a highly experimental focus, because the required understanding of key problems can only be achieved through observation. For example the way nucleation affects polymorphism is poorly understood and requires new experimental techniques, perhaps through combined spectroscopy and NMR, or in situ X-ray diffraction.

The Network has an informal structure comprising common study, and a mixture of short and long term visits, designed to foster the required experimental innovation. The Network will then conclude towards the end of its three-year period (2001-2005) with a major international conference on the study and implications of polymorphism.

This Network was approved by the ESF Network Group in November 2000 for a three-year period



Coordination Committee

**Professor Joel Bernstein
(Co-Chairman)**

*Department of Chemistry
Ben-Gurion University of the Negev
POB 653
84105 Beer-Sheva
Israel
Tel: +972 8 646 1187
Fax: +972 8 647 7641
Email: joel@bgumail.bgu.ac.il*

**Professor Roger Davey
(Co-Chairman)**

*Department of Chemical Engineering
UMIST
P.O. Box 88
Manchester M60 1QD
United Kingdom
Tel: +44 161 200 4409
Fax: +44 161 200 4399
Email: r.j.davey@umist.ac.uk*

Professor Roland Boese

*Institut für Anorganische Chemie
Universität Essen
Universitätsstrasse 3-5
45117 Essen
Germany
Tel: +49 201 183 2416
Fax: +49 201 183 2535
Email: boese@structchem.uni-essen.de*

Professor Bill David

*ISIS Facility
Rutherford Appleton Laboratory
Chilton
Oxon OX11 0QX
United Kingdom
Tel: +44 1235 44 5179
Fax: +44 1235 44 5383
Email: bill.david@rl.ac.uk*

Professor Jack Dunitz

*ETH
Universitätstrasse 16
8092 Zürich
Switzerland
Tel: +41 1 632 2892
Fax: +41 1 632 1109
Email: dunitz@org.chem.ethz.ch*

Dr. Peter Erk

*BASF AG
ZDP/F-J550
67056 Ludwigshafen
Germany
Tel: +49 621 60 414 36
Fax: +49 621 60 747 42
Email: peter.erk@basf-ag.de*

Professor Angelo Gavezzotti

*Dipartimento Chimica Strutturale e
Stereochimica Inorganica
University of Milan
Via Venezian 21
20133 Milan
Italy
Tel: +39 02 7063 5120
Fax: +39 02 7063 5288
Email: angelo.gavezzotti@unimi.it*

Dr. Ulrich Griesser

*Institut für Pharmazie
Universität Innsbruck
Innrain 52
6020 Innsbruck
Austria
Tel: +43 512 507 5309
Fax: +43 512 507 2939
Email: ulrich.griesser@uibk.ac.at*

Professor Robin Harris

*Department of Chemistry
University of Durham
South Road
Durham DH1 3LE
United Kingdom
Tel: +44 191 374 3121
Fax: +44 191 386 1127
Email: r.k.harris@durham.ac.uk*

ESF Liaison

Mr. Neil Williams

Senior Scientific Secretary

Mrs. Marie Clifford-Gruber

Administrator

Tel: +33 (0)3 88 76 71 07

Fax: +33 (0)3 88 37 05 32

Email: mclifford@esf.org

The European Science Foundation acts as a catalyst for the development of science by bringing together leading scientists and funding agencies to debate, plan and implement pan-European initiatives.

The ESF Network scheme is coordinated from the Foundation's Strasbourg headquarters. For further information and application procedures contact:

Tony Mayer

Tel: +33 (0)3 88 76 71 46 - Fax: +33 (0)3 88 37 05 32 - Email: networks@esf.org

