December 2003

SLTB Newsletter

****STOP PRESS****

Web Site Status

After many months of the SLTB web site being unavailable, the web hosting problem has now been resolved and the site can be accessed again on **www.sltb.info** (although if you use 'old' versions of the Netscape browser the pages will not format correctly on screen). The Committee has decided that Belinda Wade (Medical Cryobiology Unit, University of York) will administer the site and keep it updated in future and she is very thankful for the help of Paul Waites from Biology IT at the University of York. We hope that members will find it a useful source of information and a convenient place to exchange ideas.

Committee contact details can be found on **http://www.sltb.info/committee.htm**.

Annual Membership Fees

Please note that the annual fees of SLTB membership will be increased to **£20** for a standard member and **£15** for a student from **1st January 2004**. Since the SLTB cannot accept credit card payments, the best way of paying is by using a standing order. Members are urged to complete the Standing Order Form enclosed with this Newsletter and send it to your bank as soon as possible. Payments can also be made by cheque (any bank charges have to be covered by the payer) or in cash to the Treasurer (Tiantian Zhang) at SLTB meetings.

Report on CryoBioMol 2003

The ancient university city of Coimbra in Portugal was the site of the recent CryoBioMol meeting. Established as a collaborative enterprise between our Society (SLTB), the Society for Cryobiology, and the Low Temperature Spectroscopy Group in Coimbra, the setting was the university campus in the magnificent old quarter of the city on a hill overlooking the Mondego River. Some 170 participants gathered together for four extraordinary days of excellent science, discussion and social gatherings put together around our mutual interests in low temperature science at the opening of the 21st century. The local hosts, under the direction of Professor Rui Fausto, provided a superb programme covering a remarkably broad range of topics, ranging from the potential for life to survive in the cryogenic interstellar environment to modern-day applications of cryobiology in biotechnology and medicine. Each day was organised into a pattern of stimulatory plenary lectures followed by specialist topic presentations from the participants, a format which was well received by the audience.

The meeting was opened by an address from the University Rector, Andreas Sputtek (as Chairman of SLTB) and Mehmet Toner (as President of the Society for Cryobiology). This was followed by an exciting symposium on Life at Extreme Low Temperatures, which included presentations on the possibility that life had been seeded on Earth via cryogenic transport from across the universe by comets, and the mathematical basis of this 'panspermia'. In conjunction with a discussion on the potential for complex

life to evolve on 'Snowball Earth' during extreme glaciation, and current knowledge on the molecular basis for freeze tolerance and over-wintering in polar regions (in both invertebrates and vertebrates), these provided illuminative and provocative starting points for the rest of the conference.

On the second day, the topics covered included the most recent information on vitrification in complex biological systems, and the perspectives and limitations for applying this technology. The resurgence of interest in achieving cell and tissue preservation by drying techniques, either with or without low temperature freezing steps, was also covered. The importance of low temperature spectroscopy in undertaking the interactions of biomolecules was described in associated topic presentations. Applied low temperature technology in tissue and organ preservation was also dealt with during short topic presentations.

Subsequent plenary sessions over the next two days dealt with what have become the important practical applications of cryobiology today – cryopreservation of gametes and embryos, blood cells, the expanding horizon of stem cell technologies, and targeted destructive freezing in cryosurgery. These topics were well supported by short oral presentations from the attendees. Of particular note was the session on bioethics applied to cryobiology, where thought-provoking discussions were set out on the current global status of therapeutic cloning (which will depend heavily on cryobiological input), and ethical dilemmas in tissue donation and storage. There was a strong representation of poster communications which were grouped into topics related to the meeting plan, and the afternoon of the third day was devoted to these.

As always in meetings of our societies, strong encouragement was given to the young and upcoming scientists in our field, by travel support and competitions, both strongly contested, for the best oral and poster presentations. After lengthy and difficult committee deliberations, the prize for the oral presentation was awarded to K Snyder (Binghamton, USA) for studies on cardiomyocytes exposed to low temperatures, and for the best poster presentation to V Robles (Leon, Spain) for investigations into fish oocyte cryopreservation.

The excellent scientific fare was equalled by the magnificent social programme provided by the CryoBioMol hosts. This included a 'get together' party in a tavern on the university campus, a fine reception in the ancient Town Hall of the city, and a sumptuous banquet in a nearby castle, where guests were also treated to a concert of the Fado-style music, typical of this region of Portugal. However, just being in the environs of the ancient University was equally pleasant over the days of the meeting, and proved to be a fine atmosphere for making new friendships or renewing old collaborations in low temperature biology. The SLTB is extremely grateful to Rui Fausto and his colleagues for providing such an excellent event.

Barry Fuller, Meetings Secretary

New Committee Member: History, Thoughts and Future

It is a delight and pleasure to be elected onto the SLTB committee, if not a somewhat surprising outcome for a long-term member, to be appointed after working in plant cryopreservation for some 18 years. I can thank an ex-society chairperson, Lyndsey Withers, for the introduction to the subject of plant cryopreservation via a jointly funded (formerly) IBPGR, now the IPGRI, research programme between the University of Nottingham's departments Genetics with Agriculture and Horticulture in a pioneering endeavour to examine the genetic stability of plant genomes recovered from cryopreservation. Indeed, these were the early days of exploring applications in *in vitro* biotechnology, a theme some may recall was the subject of the SLTB meeting "Chromosomes, Genes and Cryobiology" (Oct 2002) at the Medical Society of London to address stability issues within these subjects (see Dec 2002 Newsletter).

Since those 'heady' days at Nottingham, considerable progress has been made from the use of a simple 'Southern blot' to the numerous applications in plant genomics. Nonetheless, the issues arising from the application of cryopreservation techniques (ultra-rapid, slow-rate freezing; the use of liquid droplets, alginate encapsulated beads and various vitrification solutions) to plant conservation are still subjects of debate (await forthcoming issues of CryoLetters; http://www.cryoletters.org). Many of these techniques are practical approaches to conserve germplasm and current EU-funded research programmes are active to further understand and elucidate the mechanisms of cryoinjury and genetic stability in diverse micro-algae (www.cobra.ac.uk) and a wide range of higher plants (www.agr.kuleuven.ac.be/dtp/tro/crymcept/). Undoubtedly, these EU projects will further advance applications in cryopreservation for the long-term conservation of germplasm within *in vitro* collections. Presently, I am working with Erica Benson, as a team member in the University of Abertay Dundee's Plant Conservation Group (http://scieng.tay.ac.uk/plant/index.htm). Should SLTB members require further details regarding these research activities please contact me for information.

Keith Harding
(k.harding@abertay.ac.uk)

New Members

The following members have recently joined the SLTB:

Jason Acker, Canadian Blood Services
Ganna Isayeva, University of Luton
Paul Matejtscnuk, NIBSC
Patricia M^{c}Alernon, Innovatis AG
Michèle Marin, INRA, France
Max Plachinta, University of Luton
David Stevenson
Kevin Ward, Biopharma Technology Ltd.

New member profiles

Jason Acker
(jacker@ualberta.ca)
Dr Jason Acker is an Associate Scientist with the Canadian Blood Services (CBS) and an Assistant Professor in the Department of Laboratory Medicine and Pathology at the University of Alberta, Edmonton, Canada. He received his Bachelor of Science, Master of Science in Experimental Pathology and PhD in Medical Sciences degrees from the University of Alberta. Dr Acker has recently returned to Edmonton after spending two years in Boston as a Canadian Institute for Health Research (CIHR) Post-Doctoral Fellow at the Massachusetts General Hospital and Harvard Medical School.

Cryopreservation is the process whereby biological function is maintained by freezing and storage at ultra-low subzero temperatures. Unfortunately, current red blood cell cryopreservation remains an expensive procedure that requires highly trained technicians and specialized equipment for processing and storage making it logistically prohibitive for routine use in large-scale operations. In addition, there are a number of blood components that have limited viability following cryopreservation including granulocytes and platelets. Recent advances in cryobiology research have resulted in new methods for the cryopreservation of mammalian cells using low concentrations of intracellular sugars to protect cells. Sugars have been shown to be important stabilizers of membranes, proteins and other key cellular structures in plants and animals that undergo extreme environmental stresses such as desiccation and freezing. Dr Acker's work focuses on the development of strategies for the introduction of protective amounts of intracellular sugars into human blood cells with the end goal of making cryopreservation of blood more cost effective and efficient. In addition, Dr Acker's group is working to better understand the effects of desiccation and drying on blood cell structure and function. Dry storage of mammalian cells promises to eliminate many of the problems associated with current clinical cryopreservation, providing a more effective method for the ambient temperature, long-term storage of blood cells.

In addition to his work in biopreservation, Dr Acker has an active research interest in the use of microfabrication and microfluidics technology in diagnostic testing. Using tools developed for the microelectronics industry to fabricate micro-scale devices for integrated chemical and biological processing and analysis, the research group in Edmonton is developing novel, cost-effective, automated devices for blood testing. This lab-on-a-chip technology will contribute to reducing human-related errors while providing rapid, high-throughput results. By developing the expertise and resources necessary to build micro-devices, Dr Acker is providing an important resource for other CBS scientists and staff interested in using this technology in their own research programs.

Kevin Ward
(KWard@biopharma.co.uk)
Following a BSc in Applied Chemistry, Kevin was awarded his PhD for research into freeze-drying technology at Aston University, Birmingham, where he investigated many aspects of the technology including the behaviour and protection of proteins and stealth liposomes during lyophilisation. Kevin has since worked at Pfizer in Sandwich, Kent, where he was involved with a number of projects within the Dept of Pharmaceutical R&D. He then returned to Aston University to take up a Research Fellowship in the Vaccine Development, where he worked on freeze-dried vaccines for single-dose oral and nasal delivery.

Kevin joined Biopharma Technology in March 2000, where he is currently R&D Manager. Biopharma is involved almost exclusively in freeze-drying R&D, so Kevin's interest in low temperature biology centres on the behaviour of materials upon freezing and around their characteristic eutectic, glass transition and/or collapse temperatures. This includes the analytical study of - and process development for - formulations for therapeutics, vaccines and diagnostics, amongst others. Kevin has written several published articles and has been an invited speaker at a large number of conferences, both in the UK and internationally.

Patricia McAlernon
(Patricia.McAlernon@innovatis.com)
Dr Patricia McAlernon is the UK Sales Agent for Innovatis AG (www.innovatis.com) who manufactures the Cellscreen and the Cedex automatic cell counter. Dr McAlernon is investigating the possibilities of using the Cellscreen in conjunction with the Incubatrix 96 supplied by Linkam Scientific Instruments (www.linkam.co.uk) for cryogenic studies. The combined system will allow cell size to be determined in microwell plates without the need for staining and sampling.

SLTB Annual Meeting 2004

The Annual meeting will be held in London at the Royal Free Hospital, hosted by Barry Fuller and colleagues, on September 9th and 10th 2004. The two day event will include a symposium on "Cryopreserving Hepatocytes", an area of renewed interest with the recent application of novel cell-based therapies and biotechnological applications. There will also be Free Communications Sessions, Prize Presentation Sessions for younger members of SLTB, Poster Sessions, and the AGM of the Society. The Annual Dinner will be held in one of the nearby excellent restaurants in Hampstead. More details will be sent early in the New Year. Make a note in your diary now, and be prepared to enjoy good science and London life next autumn!

Jacobus Henricus van't Hoff

(1852-1911)
First Nobel Prize Winner in Chemistry
(1901)

Through the use of the Boyle-van't Hoff relationship (a plot of cell volume vs. 1/osmolality), it is possible to determine the osmotically active water content of biological cells. Whereas much is known about Robert Boyle (born: 25th January, 1627 in Lismore, County Waterford, Ireland, died: 30th December, 1691 in London, England), who was van't Hoff?

Jacobus Henricus van't Hoff was born in Rotterdam, The Netherlands, on 30th August, 1852. He was the third child in a family of seven children of Jacobus Henricus van't Hoff, a physician, and Alida Jacoba Kolff. In 1878 he married Johanna Francina Mees. They had two daughters, Johanna Francina (1880) and Aleida Jacoba (1882) and two sons, Jacobus Hendricus (1883) and Govert Jacob (1889). He died on 1st March, 1911, at Steglitz near Berlin.

In 1869 he entered the Polytechnic School at Delft and obtained his technology diploma in 1871. His decision to follow a purely scientific career, however, came soon afterwards during vacation-work at a sugar factory when he anticipated for himself a dreary profession as a technologist. After having spent a year at Leiden, The Netherlands, mainly for mathematics, he went to Bonn, Germany, to work with AF Kekulé from autumn 1872 to spring 1873; this period was followed by another in Paris with A Wurtz, when he attended a large part of the curriculum for 1873-1874. He returned to Holland in 1874 and obtained his doctor's degree that same year under E Mulder in Utrecht.

In 1876 he became lecturer at the Veterinary College at Utrecht, but left this post for a similar position at the University of Amsterdam the following year. In 1878 came his appointment as Professor of Chemistry, Mineralogy, and Geology at the same university. Having occupied this chair for 18 years he accepted an invitation to go to Berlin as an Honorary Professor, connected with membership of the Royal Prussian Academy of Sciences. He remained at this post until the end of his life. The principal reason for this change was the fact that he was overburdened with obligations to give elementary lectures and examinations for large numbers of students, leaving him with too little time to do his own research work. He was an ardent advocate for the creation of a special class of scientific workers.

van't Hoff has acquired fame particularly for his epoch-making publications. His doctoral thesis (1874) was entitled "Bijdrage tot de Kennis van Cyaanazijnzuren en Malonzuur" (Contribution to the knowledge of cyanoacetic acids and malonic acid). Of far greater weight, however, was his publication which appeared several months before: "Voorstel tot Uitbreiding der Tegenwoordige in de Scheikunde gebruikte Structuurformules in de Ruimte, etc." (Proposal for a 3-dimensional extension of the presently used chemical structural formulae, etc.). This small pamphlet, consisting of twelve pages of text and one page of diagrams, provided the impetus for the development of stereochemistry. The concept of the "asymmetrical carbon atom", dealt with in this publication, supplied an explanation of the occurrence of numerous isomers, inexplicable by means of the then current structural formulae. At the same time he pointed out the existence of the relationship between optical activity and the presence of an asymmetrical carbon atom.

His revolutionary ideas only found acceptance after the publication, in 1875, of his "Chimie dans l'Espace"; especially when two years later the German translation appeared, with an introduction by J Wislicenus. (The English translation: "Chemistry in Space" did not appear until 1891.) In his "Dix Années dans l'Histoire d'une Théorie" (Ten years in the history of a theory) he drew attention to the fact that JA Le Bel had independently arrived at the same ideas, though in a more abstract form.

In 1884 his book "Études de Dynamique chimique" (Studies in dynamic chemistry) appeared, in which he entered for the first time the field of physical chemistry. Of great importance was his development of the general thermodynamic relationship between the heat of conversion and the displacement of the equilibrium as a result of temperature variation. At constant volume, the equilibrium in a system will tend to shift in such a direction as to oppose the temperature change which is imposed upon the system. Thus, lowering the temperature results in heat development while increasing the temperature results in heat absorption. This principle of mobile equilibrium was subsequently (1885) put in a general form by Le Chatelier, who extended the

principle to include compensation, by change of volume, for imposed pressure changes - it is now known as the "van't Hoff-Le Chatelier principle".

"L'Équilibre chimique dans les Systèmes gazeux ou dissous à l'État dilué" (Chemical equilibria in gaseous systems or strongly diluted solutions) followed in 1885, which dealt with this theory of dilute solutions. Here he demonstrated that the "osmotic pressure" in solutions, which are sufficiently dilute, is proportionate to the concentration and the absolute temperature so that this pressure can be represented by a formula which only deviates from the formula for gas pressure by a coefficient "i". He also determined the value of "i" by various methods, for example by means of the vapour pressure and Raoult's results on the lowering of the freezing point. Thus van't Hoff was able to prove that thermodynamic laws are not only valid for gases, but also for dilute solutions. His pressure laws, given general validity by the electrolytic dissociation theory of Arrhenius (1884-1887) - the first foreigner who came to work with him in Amsterdam (1888) - are considered the most comprehensive and important in the realm of natural sciences.

WJV Osterhout (1871-1964), an emeritus member of the Rockefeller Institute, reported the story of the discovery as follows to Nobel laureate George Wald, Professor Emeritus of Biology at Harvard University (who wrote it down): One day in Amsterdam, Jacobus Henricus van't Hoff, the "father of physical chemistry", was walking down the street from his laboratory when he encountered his fellow professor, the botanist Hugo de Vries, out walking with his wife. Having met, they went on together, whereupon de Vries ventured, "The other day I had a letter from Pfeffer" [Wilhelm Pfeffer (1845-1920), the botanist who pioneered the use of semipermeable membranes to measure osmotic pressure]. When van't Hoff inquired in the desultory Dutch equivalent of "Oh, yeah? What's he up to?" de Vries replied, "He says he's measuring the effect of temperature on osmotic pressure." "What does he get?" asked van't Hoff. "Well," replied de Vries, "he writes that for each degree rise in temperature the osmotic pressure goes up by about 1/270." That did it, for van't Hoff immediately recognized 270 to be an approximation of the absolute temperature, 273 K at 0°C. By that night van't Hoff was well launched on the theory of ideal solutions, with its fundamental equation the exact equivalent of the ideal gas law, $pv = RT$, becoming in dilute solutions $p/c = RT$, in which "p" is now the osmotic pressure, "c" the concentration, "R" the universal gas constant, and "T" the absolute temperature.

During his Berlin period, from 1896 to 1905, van't Hoff was continuously engaged on the problem of the origin of oceanic deposits. In this extensive work he was especially assisted by W Meyerhoffer, who had previously worked with him in Amsterdam for a number of years. He was probably the first to apply small-scale results, obtained in the laboratory, to phenomena occurring on a large scale in nature. The results of this ambitious investigation, mostly published in the proceedings of the Prussian Academy of Sciences, were summarized by him in a two-volume work "Zur Bildung ozeanischer Salzablagerungen" (1905-1909).

van't Hoff greatly valued the power of imagination in scientific work, as is apparent from his inaugural address on taking up his professorship in Amsterdam: "Verbeeldingskracht in de Wetenschap" (The power of imagination in Science), in which, after a rather elaborate study of biographies, he arrived at the conclusion that the most prominent scientists have possessed this quality in a high degree. Wilhelm Ostwald and van't Hoff who together established the "Zeitschrift für physikalische Chemie" (Journal for Physical Chemistry) in Leipzig, Germany, can be regarded as the founders of physical chemistry.

Of the numerous distinctions he himself mentioned, his award of the first Nobel Prize in Chemistry (1901) was the culmination of his career. In 1885 he was appointed a member of the "Royal Netherlands Academy of Sciences", after his nomination had been withheld in 1880 because of an insufficient number of votes - a proof that his ideas initially found little acceptance in his own country. Among his

other distinctions were the honorary doctorates of Harvard and Yale (1901), Victoria University, Manchester (1903), Heidelberg (1908); the "Davy Medal of the Royal Society" (1893), "Helmholtz Medaille der Preussischen Akademie der Wissenschaften" (1911). He was also appointed "Chevalier de la Légion d'Honneur" (1894) and "Senator der Kaiser-Wilhelm-Gesellschaft" (1911). He was a member or honorary member of the Chemical Society, London (1898), Koenigliche Akademie der Wissenschaften, Goettingen (1892), American Chemical Society (1898), and Académie des Sciences, Paris (1905).

van't Hoff was a lover of nature; as a student in Leyden he frequently took part in the botanical excursions, and later in Bonn he fully enjoyed the mountains in the vicinity, taking long walks in company or alone. His quite detailed description of his journey to the United States, resulting from an invitation to lecture at Chicago University, amply shows his love of travel. His receptiveness for philosophy and his predilection for poetry were already apparent in his early school years - Lord Byron was his idol.

Compiled from various internet sources, with minor changes, including:

http://www-gap.dcs.st-and.ac.uk/~history/Mathematicians/Boyle.html
http://www.nobel.se/chemistry/laureates/1901/press.html
http://urila.tripod.com/
http://www.nobel.se/chemistry/laureates/1901/hoff-bio.html
http://scienceworld.wolfram.com/biography/vantHoff.html
http://www.chemheritage.org/EducationalServices/chemach/cssb/jhh.html
http://dbhs.wvusd.k12.ca.us/Chem-History/vantHoff.1887.html
http://www.1upinfo.com/encyclopedia/V/vantHoff.html

Andreas Sputtek

Charity Status

The Society is now a Registered Charity - in fact we are now charity number 1099747. The trustees comprise the elected committee and the new Constitution is on the Society's website at www.sltb.info. The wording of our Objects clause is particularly important because this is now the legal definition of our purpose as a charity. This really only puts into formal wording the purposes we have always had - to educate the public in the science of low temperature biology, to advance and promote research in that science and to disseminate research results for the general good. Charitable status does impose certain disciplines upon the Society with respect to record keeping, financial management and constitutional arrangements. As a charity, the Society will in future be able to recover the tax element on subscriptions and donations and will therefore be better financed to achieve its objectives. For this to take effect, the Society now has to register with the Inland Revenue. This is in hand, and when all the details are known the Treasurer will set them out.

David Pegg

Obituary

It is with great sadness that we announce the death on November 18th 2003 in Marseille of Gisèle Novakovitch. Gisèle was a well known and highly respected figure in European tissue banking and a pioneer of cryobiology in France. She also became known to members of the SLTB through her key role in the organization of the joint meeting of the SLTB, France CRYO and Society for Cryobiology in Marseille in 1999. Thanks to her energy and commitment, this meeting was a great success, both scientifically and socially.

Gisèle's contribution to the theory and practice of tissue banking was twofold: both through basic cryobiological research in to the preservation of a number of tissues (nerves, bone, heart valves, blood cells, bone marrow) and through commitment to improvements in the collection and preservation of human tissue for transplantation. She championed the importance of standardisation, was always open to new therapeutic applications and receptive to the needs of her clinical colleagues. However she always regarded the needs of her patients

as paramount.

Gisèle studied medicine in Marseille and then joined the Etablissement Français de Sang (Blood Donor Service) where her interests soon became focussed on the improvements in methods for bone marrow preservation and, in particular, platelet collection by apheresis. Her enthusiasm for the subject led her, at the end of the 1980s, to become a founder member of France CRYO of which she was President for a number of years. She became the driving force behind the Ethical Committee on Human Tissue Transplantation, encouraging debate on control, regulation and ethics of human cell transplantation, and advised the government on cell therapy protocols. This led to involvement in the Etablissement Française des Greffes, created in 1995 to govern the clinical transplantation of organs, tissues and cells, an involvement which took her to Paris on a part time basis.

Gisèle's enthusiasm and energy spilled over into involvement in local politics in her home village of Grambois where she was a councillor and mayoral candidate. Here she was instrumental in the creation of an infant day-care centre and a club for young mothers in order to attract newcomers to the village. She was also totally devoted to her family, husband Yves and sons Frederic and Pierre. Weekends at home with her family were her priority, but her home was always open to visitors who were made to feel totally welcome by the warmth of her hospitality. Barry Fuller and I can remember the day spent in her home in 1998 when, following an arduous day spent planning the scientific programme, Gisèle disappeared into the kitchen with her family to produce a delicious French country meal with local wine for the whole scientific committee.

Her colleagues and friends remember Gisèle as a person with outstanding professional skills and enthusiasm, but also as a warm hearted individual widely respected for her courage and integrity. She will be sadly missed. We send our condolences to her friends and colleagues and, above all, to her family.

Monica Wusteman
(With thanks to Maryna Blankenstein-Gabert, Isabelle Desbois and Anne Baudot for their help in preparing this.)

Request for Email Addresses

To help improve communication with the membership we want to develop a database of all members' email addresses. The intention is not to replace the traditional Society Newsletter with an electronic version, but rather to supplement it with specific news items etc. which we wish the membership to be aware of between the publication of Newsletters. Would you please send your email address to the General Secretary at **P.T.Lynch@derby.ac.uk**. Sending it electronically will save him lots of typing, and the inevitable mistakes.

Thank you to those members who responded to the request for email addresses in the last Newsletter.

Note: The material for this edition was prepared by Andreas Sputtek.