AuPS News

President's Message

The upcoming joint AuPS meeting to be held in Melbourne 30th November – 3rd December promises to be an outstanding meeting with numerous distinguished national and international speakers giving Plenary Lectures or participating in Symposia. A Plenary Lecture is to be given by Professor Lars Larsson (Uppsala University, Sweden), the UK Physiological Society Visiting Lecturer is Professor Colin Sibley (University of Manchester, UK) and the AuPS Invited Lecture is to be delivered by Professor Graham Lamb (La Trobe University). The meeting will also be an occasion to recognise four eminent physiologists (Professor Elspeth McLachlan, Professor Geoffrey Burnstock, Professor Colin Gibbs and Professor Uwe Proske) by election to Honorary Membership of AuPS for their contributions to the Society and physiology in Australia. The AuPS Council welcomes nominations of members for election to Honorary Membership in recognition of their significant contributions to the Society and physiology research and teaching in Australia.

The Cutler Review of Innovation has just been released and it will be of interest to follow the impact this has on research funding in Australia. The review has called for an urgent $2.2 billion annual increase for research at universities and, in particular, recommends rapid transition to funding the full cost of research at a time when grants usually cover less than half of a university's research cost on a project. Other recommendations include raising the annual stipend for Australian Postgraduate Award students to at least $25,000 and extending its duration to 4 years.

I wish to encourage members to attend the 36th International Congress of Physiological Sciences (IUPS) which will take place in Kyoto, Japan 27 July - 1 August 2009. This information is available on their website http://www.iups2009.com/ where registration and abstract submission is now open. Abstract submission is from September 1 until December 10, 2008. There is also the information about travel grants on the site. The planning of the 2010 Annual Meeting and 50th Anniversary of AuPS to be held jointly with the Australian Neuroscience Society (ANS) at the Sydney Convention Centre (31st January – 3rd February, 2010) is progressing and I am delighted to announce that Professor David Atwell, University College London, will be the Physiological Society (UK) Exchange Lecturer.

Finally, I wish to thank the Local AuPS Organising Committee and in particular the Local Secretaries, Gordon Lynch and Graham Lamb, for putting together an excellent scientific and social programme. I encourage all members, including student members, to attend the AuPS Annual General Meeting at and become involved in the activities and future of **your** professional society..

The AuPS Scientific Meeting
The University of Melbourne, Parkville
30th November – 3rd December 2008

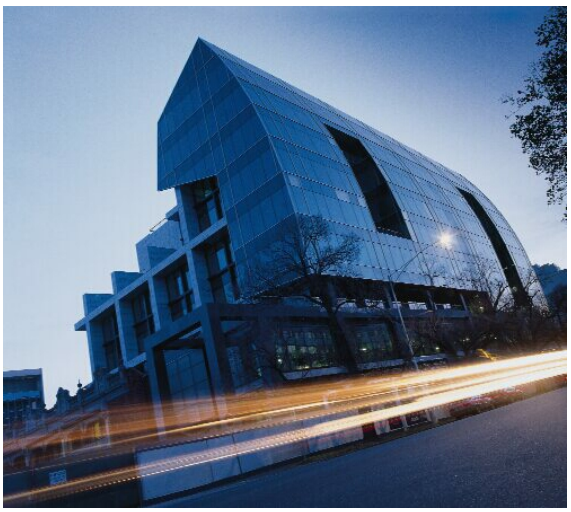
The 2008 AuPS annual meeting will be held at the Parkville campus of The University of Melbourne. The Conference proceedings will take place in several spacious lecture theatres in the tri-radiate Medical Building of the Faculty of Medicine, Dentistry and Health Sciences. It will include presentations from leading national and international scientists in the fields of cardiac muscle, skeletal muscle and exercise physiology, ion channels and electrophysiology, cardiovascular physiology, metabolism and diabetes, neuroscience and molecular physiology. The meeting will include plenary lectures, symposia, free communications, poster sessions and trade displays.

There is a special focus on students; offering opportunities to showcase Ph.D. research, to participate in symposia related to research fellowships and career development, and to meet other students in the related social activities.

WELCOME RECEPTION

The welcome reception will be held in the impressive Alan Gilbert Building in University Square, directly opposite the Medical Building on Grattan Street. This award winning building, completed in 2003, is conveniently located a short walk from the main lecture theatres. The welcome reception will be an evening to enjoy networking and social discussions over a selection of finger food and beverages.

Date: Sunday November 30th
Time: 6pm – 8pm
Venue: Alan Gilbert Building,
Executive Lounge



161 Barry Street (corner of Grattan St.)
Carlton, 3010 .

General enquiries please contact:
The Local Secretary

Gordon S. Lynch
Department of Physiology
The University of Melbourne
Victoria, 3010, AUSTRALIA

DON'T MISS THESE IMPORTANT DEADLINES

-Abstracts: 26th September, 2008

-Early Registration: 26th September, 2008

Call for Abstracts
The online registration and abstract submission system is now open for the Melbourne scientific meeting. Please note that the deadline for acceptance of abstracts is **26 Sep 2007**

Early Registration Deadline: Close of business, 26th Sept.
A late registration levy of $50 applies to all participants if registrations are made after this date
Registration Fees Include:

- access to all sessions
- welcome reception on Sunday evening
- student mixer on Monday evening
- lunches Monday to Wednesday
- morning/afternoon teas

Fees (early registration)

- Full member: $320
- Student member $160
- Full non member $450
- Student non member $290

Honours student presenters (non members) $160

It will be cheaper to join and register as a member than to register as a non-member. You can apply for membership on-line. If you apply, please wait for your membership confirmation email before starting to register to obtain the membership registration fee.

Conference Dinner
Please note that places for the conference dinner are limited to 150
The 2008 conference dinner will be held at University House – the private dining and function centre at The University of Melbourne. University House is also conveniently located on the Parkville campus and is a short walk from the Medical Building. Dating back to 1885, University House is the sole survivor of a number of beautiful Victorian homes that were built for the original founding Professors of the University and which once lined Professor's Walk.
A short stroll from the conference proceedings through the University gardens will see you at the conference dinner in less than two minutes.
When: Tuesday December 2nd, 2008
Time: 6.30pm start
Where: University House, The University of Melbourne.
Cost: $85 per person $50 for students

Key Lectures

Plenary Speaker

Professor Lars Larsson, MD, PhD

Uppsala University, Sweden

Regulation of human muscle contraction in health and disease

AuPS Lecture

Professor Graham Lamb,

La Trobe University, Australia

Summaries of Symposia are detailed throughout the Newsletter

Ion Channels as Therapeutic Targets for Multiple Diseases

Organiser: David Adams

Novel approaches for screening sodium channel function in drug discovery
Steve Petrou Howard Florey Institute

Translational promise and physiological insights in Aquaporin drug discovery
Andrea Yool University of Adelaide

The capsaicin receptor TRPV1, as a target for chronic pain therapy
Peter McIntyre University of Melbourne

The Purinergic P2X7 channel/pore and Mood Disorders
Jim Wiley University of Sydney

Myopathies and Muscle Regeneration

Organiser: Gordon Lynch

Using gene transfer technology to study muscle diseases
Paul Gregorevic The Baker Heart Research Institute

Muscle hypertrophy and IGF-1 isoforms: is bigger better?
Thea Shavlakadze University of Western Australia

Novel regeneration in nemaline myopathy
Anthony Kee Children's Medical Research Institute, Westmead

Acute Quadriplegic Myopathy in ICU patients: Underlying mechanisms and intervention strategies.
Lars Larsson Uppsala University, Sweden

A brief biography by Prof. Graham Lamb. Presenter of The AuPS lecture in 2008.

Although I have been working in cellular physiology of skeletal and cardiac muscle for longer than I care to remember (25 years now), some whole animal neurophysiologists and others might remember that I actually started out in physiology doing my postgraduate studies in the somatosensory system, comparing psychophysical measurements in humans with peripheral recordings of touch receptors in the monkey, trying to understand the basis of texture discrimination. I actually did my undergraduate work in physics, maths and chemistry, and had never done any biology at all (some may think that shows!) until I jumped into doing an Honours year in Physiology with Ken Johnson and Ian Darian-Smith at the University of Melbourne. It was a great move, because the brain had always fascinated me and it was a high quality and friendly lab. I made another shift at the end of my PhD, joining Peter Gage and Angela Dulhunty at University of NSW and then ANU, another great move, taking me into cell physiology and biophysics. I was fortunate enough to get a QEII Fellowship, which was unusual back then because they were typically awarded only to people returning to Australia. I think there was a bit of a cultural cringe back then too, with the thinking being that one could only get top level experience at an overseas institution, which I always thought odd given the world-class research done here. In 1988, I moved to La Trobe University to take up an NHMRC Research Fellowship. In those days you couldn't apply for an NHMRC grant and coupled Fellowship on your own, as you had to apply for the grant jointly with a university academic or already be a Fellow, which was certainly a bit of a catch-22. The tremendous upside of this was that it started me in my long-standing and fruitful collaboration with George Stephenson, which among other things took me into the mysterious world of skinned muscle fibres. All up, I feel that I have been very fortunate to work in physiology and with so many first rank scientists. When I lecture to undergraduate students in membrane physiology, I tell them that physiology is not a matter of rote-learning but of understanding mechanisms, and that makes it a whole lot simpler to remember and much more satisfying! In finishing, I'll just mention my memory of awaiting the outcome of the editorial deliberations on my first ever manuscript and reading in the newspaper of the comments of Dr Samuel Johnson, the 18th century writer, critic and editor, who wrote to a hapless author: "Thank you for your manuscript, which is both good and original. Unfortunately what's good is not original and what's original is not good". Luckily the reviewers and editor were kinder about my manuscript.

Signals mediating exercise-induced skeletal muscle remodelling

Organiser: Mark Hargreaves

Histone modifications and skeletal muscle metabolic gene expression
McGee University of Melbourne

Molecular regulation of skeletal muscle mass
Aaron Russell Deakin University

Calpains and skeletal muscle function
Robyn Murphy La Trobe University

A novel role for beta-adrenoceptor signalling in the regulation of skeletal muscle mass

James Ryall NIAMS/National Institutes of Health

Role of ROS in cardiovascular function and disease

Organisers: Livia Hool and David Allen

ROS functions in the endothelium
Grant Drummond.

Cross talk between the L-type calcium channel and the mitochondria
Livia Hool The University of Western Australia

ROS and cardiac hypertrophy
Lea Delbridge University of Melbourne

NADPH oxidase: role in muscular dystrophy
Nick Whitehead University of Sydney

STUDENT TRAVEL AWARD

Jenny Fung won, one of the AuPS $500 travel awards to support student members and will present the following abstract in Beijing.

Molecular Mechanism Linking Acute Ethanol Exposure in Early Pregnancy to Memory Deficits in Offspring: Protective Role of Dietary Zinc Supplementation.

Jenny Fung, [1,2] Allan Rofe [2] and Peter Coyle, [2] [1]Department of Physiology, School of Molecular & Biomedical Science, University of Adelaide, SA 5000, Australia and [2]Hanson Institute and Division of Clinical Biochemistry, Institute of Medical and Veterinary Science, SA 5000, Australia

Congratulations Jenny, have a great time and travel well!

Colin Sibley – UK/Australia Visiting Lecturer for 2008: Some Background.

As the rain beats against my office window during another typical August in Manchester,

I cannot help but look forward with great excitement to my trip to Australia later this year as the Physiological Society's Visiting Lecturer. This short article is to provide members of the Australian Physiological Society with some background to the person they are getting this year and also my plans for the trip.

I am a Londoner by birth and early training. My first degree (in Biochemistry and Physiology) and PhD were obtained from Queen Elizabeth College in the University of London. The latter was a study of steroid secretory mechanisms in the rat adrenal cortex but, finding myself facing unemployment at the end of my PhD, and having just married, I jumped at an offer of a postdoctoral position at St. Georges Hospital Medical School, to work with Tony Firth on the guinea pig placenta. This was a life changing move as the rest of my career has been in the study of the physiology of the placenta, in relation to fetal growth and some of the main diseases in pregnancy, fetal growth restriction and pre-eclampsia. Nearing the end of my three years at St. Georges I applied for a Lectureship at the University of Manchester in the Department of Child Health headed by Robert Boyd who is both a paediatrician and placental physiologist. The advert stated that expertise in the physiology of the placenta was highly desirable for the appointment, which must have cut down the competition somewhat, and I started as Lecturer in Child Health and Physiology at the University of Manchester in September 1982. The appointment was quite novel for its day as it was joint between the Department of Child Health, where my research was based, and in the Department of Physiology (under Maynard Case) where my teaching was based. Having one foot in the clinical department and one foot in the basic science department provided me with the ideal training and experience foundation on which to develop my career in pregnancy research.

In 1989 I was awarded a Harkness Fellowship to spend a year with my wife (and by then

two children) in the USA where I worked with Irving Boime in the Department of Pharmacology at Washington University Medical School in St. Louis. I had chosen to work with Irv as he was a pioneer of applying molecular biology approaches to the study of glycoprotein hormones in general and specifically in relation to human chorionic gonadotropin production by placental trophoblast cells. I was therefore able to add a molecular perspective to my physiology: this was an enormous boon when I arrived home as at that time any grant that did not mention DNA or RNA was seemingly automatically rejected. I am pleased to say that, in the UK at least, things have now gone full circle and my physiology (or should I say integrative biology) expertise is now back in full vogue!

I was appointed Senior Lecturer shortly after my return home in 1990, and Professor of Child Health and Physiology in 1997. Shortly after my Chair appointment I was asked to take on an administrative role in the Faculty which lead eventually to a six plus year stint as Associate Dean for Research in the Faculty of Medical and Human Sciences, which finished at Xmas last year. This was a very busy time, particularly as I was responsible for the Faculty return to the UK Research Assessment Exercise, completed in November of last year. As welcome reward I am now having a sabbatical year to really concentrate on my research programme, so that the UK/Australia Visiting Lecturership has come at an ideal time.

Poor growth of the fetus whilst in the uterus can lead to prenatal or postnatal death or lifelong handicap. Furthermore, babies that are born small are at much greater risk of cardiovascular disease and of diabetes, as well as of a range of other diseases, in adulthood. The placenta is essential for allowing normal growth of the fetus. My research is focused on trying to understand how the placenta normally allows nutrients to get to the fetus and how it extracts waste products of metabolism from the fetus. Furthermore, my group has been trying to find out why the placenta is at fault in some cases of poor fetal growth; our human data show that amino acid transport abnormalities are important in this regard and work with genetically modified mice (particularly knockouts of the insulin-like growth factor gene) has shown the importance of maldevelopment of the permeability properties of the trophoblast exchange barrier. Our work is aimed at developing new ways of diagnosing women at high risk of pregnancy complications, as well as developing therapies for pregnancy disease, of which there are currently woefully few. We have recently begun a study of magnetic resonance imaging to measure placental permeability properties in women with `placental diagnostics' in mind. My group's work spans the study of cells and tissues and of the whole human placenta in the laboratory, through the study of mouse pregnancy, to the clinical studies, with close involvement of obstetrician colleagues, especially Philip Baker.

As well as leading my own research group, I am currently Director of the wider Maternal and Fetal Health Research Centre in Manchester (http://www.medicine.manchester.ac.uk/research/groups/maternalfetalhealth/). This has long term underpinning funding from Tommy's:The Baby Charity which has enabled us to develop a multidisciplinary group of 70-80 scientists, clinician-scientists and research midwives at every stage of their careers. The Centre has a focus on pre-eclampsia, fetal growth restriction and pre-term birth with colleagues utilising a variety of approaches to investigate the way the placenta forms in early pregnancy and blood flow and blood vessel physiology in mother, placenta and baby. Systems biology, as well as imaging, approaches are being taken to develop new diagnostic paradigms. We also take a special interest in the problems of our local community related to lifestyle: teenage pregnancy and obesity, both associated with a much increased risk of poor pregnancy outcome, are a current particular focus.

My wife Maureen is joining me on the trip to Australia (my third visit, her first) and we are combining work and pleasure. We are going to Vietnam on the way before heading to Sydney, where Maureen has relatives, then on to Melbourne for the AuPS meeting and a visit to Mary Wlodek at the University of

Melbourne. We are then driving to Adelaide where I will be spending time with Julie Owens, Clare Roberts and many other placental and fetal biologists at UoA. Finally we go to Perth where I plan to meet up with John Newnham and Brendan Waddell at UWA. I am looking forward to many conversations on the interaction between placental function and fetal development and the consequences for long term programming of physiological systems. We might even squeeze in some discussion on important sporting issues: I am a big Manchester United fan (though my wife is true to her roots and favours Arsenal), love cricket and we have been delighted by the success of Team GB at the Olympics!

Cardiac growth and ageing

Organisers: Lea Delbridge and John Headrick

Cardiac excitation-contraction coupling and ageing
Susan Howlett Dalhousie University, Canada

Cardioprotective signalling in aged ischemic hearts
John Headrick Griffith University

PI3K and adaptive growth in the heart
Julie McMullen Baker Institute

Metabolic challenges for cardiac mitochondria: from womb to tomb
Salvatore Pepe Murdoch Children's Research Institute

Skeletal Muscle: an Endocrine Organ

Organiser: Mark Febbraio

PGC-1α in muscle links metabolism to inflammation.
Christoph Handschin University of Zurich, Switzerland

Role of protease-activated receptors (PARs) in muscle inflammation and cytokine release
Anthony Bakker University of Western Australia

Myokines and metabolic regulation
Mark Febbraio Baker Institute

SDR CLINICAL TECHNOLOGY

SDR Clinical Technology is pleased to announce its appointment as an Australian distributor for **ImpediMed** who manufactures instruments for Body Composition and Fluid Status measurements using bioimpedance spectroscopy.

SDR will be the exclusive distributor for their latest product, ImpediVET, designed for monitoring the body composition of animal subjects. This is a single channel, tetra polar bioimpedance spectroscopy (BIS) device that scans 256 frequencies between 4 kHz and 1000 kHz in less than a second. The ImpediVET utilises Complex Impedance Plotting to determine total body water (TBW), extracellular fluid (ECF) and intracellular fluid (ICF) from impedance data. Fat-free mass (FFM) and fat mass (FM) are then calculated. The ImpediVET can be used on multiple species with the use of pre-programmed species information as well as having the flexibility to enter user-defined species information.

SDR will also sell ImpediMed medical devices that measure the same parameters in humans, generate comprehensive reports and allow further data analysis with the supplied software.

ImpediMed was incorporated to commercialise bioimpedance technologies developed by the University of Queensland and the Queensland University of Technology. These are aimed at monitoring fluid, therapeutic and nutritional states.

For further information please contact SDR Clinical Technology on 02 9958 2688 or sdr@sdr.com.au.

The Annual Meeting is when our Physiological Society awards the following annual prizes.

The A K McIntyre Prize, named in honour of the Society's first President.

The Prize shall be awarded periodically to members of the Society who are judged to have made significant contributions to Australian physiological science over their pre-doctoral and early post-doctoral years.

Nominees must be financial Ordinary Members of the Society, and must normally have completed their PhD or equivalent doctoral degree not more than 5 years prior to the time of their nomination. Nominees must be proposed by two financial members of the Society, who should provide a statement of not more than 500 words summarising the nominee's achievements. The nominee should also provide a curriculum vitae and a list of published works, including conference proceedings.

The Prize shall consist of a medal and the sum of $1000.

AuPS postdoc publication prize

An annual $500 award for the best original paper published by an AuPS member during their first 4 postdoctoral years.

Conditions for entry:

- You must be a current AuPS member.
- The paper must be on work carried out and published during your first 4 postdoctoral years.
- The paper must have been published (either on paper or online) between 30th September 2007 and 1st October 2008.
- The award should be used to present work at a conference.

Winners will be reimbursed after providing a copy of an invoice of conference expenses.

- Applications should include the following:
- A pdf of the publication,
- A statement of date of award of your PhD,
- A short statement on the paper's impact, and
- An explanation of your contribution (to multi-author papers only)

The closing date for applications is 31st October 2008.

AuPS PhD student publication prize

An annual $500 award for the best original paper published by an AuPS member during the course of their PhD studies.

Eligibility Criteria:

- You must be a current AuPS member.
- The paper must be based on work carried out during your PhD and accepted for publication within one year of the award of your PhD.
- The paper must have been published (either on paper or online) between 30th September 2007 and 1st October 2008.
- The award must be used to present work at a conference. Winners will be reimbursed after providing a copy of an invoice of conference expenses.

Applications should include the following:

- A pdf of the publication,
- a statement of date of award of your PhD,
- a short statement on the paper's impact, and
- an explanation of your contribution (to multi-author papers only)

Email all applications to:

A/Prof Joe Lynch,
School of Biomedical Sciences,
University of Queensland,
Brisbane, QLD 4072
secretary@aups.org.au

Membership general information

The subscription is currently AUD 100 per annum for full members and AUD 60 per annum for overseas members. Student members are charged AUD 100 on joining and this provides membership for up to 4 years. Financial members who retire can retain their membership without further subscriptions by notifying the Society of their retirement.

Student Presentation Prizes

In 1990, the Society instituted the awarding of prizes at each meeting for the best presentations (oral and poster) by graduate students in physiology and related disciplines.
These are at present sponsored by SDR Clinical Technology and by Blackwell Scientific.

Publications: First and second prizes in both categories are normally awarded
Eligibilty:

- Only persons who have been approved as Student Members will be eligible for Student Prizes.

Application:

- Student presenting authors need only indicate they wish to be considered for the presentation prizes when they submit their abstract through the on-line system.

In last year's competition;

Dr Renae Ryan won the award for best postdoctoral publication.
Joshua Edwards and Yang Zhe shared the award for best student publication.
PhD student prize: http://www.aups.org.au/Prizes/PhDpublication.html
Postdoc prize: http://www.aups.org.au/Prizes/PostDocPublication.html

Signaling in cell secretion

Organiser: Chen Chen and Peter Thorn

Complex interactions between ghrelin and obestatin in the regulation of GH secretion and food intake: does obestatin really exist?
Jacques Epelbaum University of Paris

Integrating studies of proteins and lipids: dissecting the mechanism of Ca^{2+}-triggered membrane fusion
Jens Coorssen University of Western Sydney

The behaviour and control of post exocytic vesicles
Peter Thorn University of Queensland

Receptor- and metabolite-mediated increase in [Ca2+]i in pancreatic islet cells by free fatty acids
Chen Chen University of Queensland

Signaling in smooth muscles

Organisers: James Brock and Dirk van Helden

Ca^{2+} phase waves - a fundamental mechanism underlying propagation of gastric slow waves
Dirk van Helden University of Newcastle

Spontaneous electrical and Ca signals underlying the autorhythmicity that drives pyeloureteric peristalsis
Richard Lang Monash University

Molecular and biophysical properties of smooth muscle-type voltage-gated Na^+ channels
Noriyoshi Teramoto Kyushu University, Japan

Do K+ channels play a role in noradrenergic signalling in vascular smooth muscle?
James Brock Prince of Wales Medical Research Institute

Epithelial Cell Biology

Organisers: Stefan Bröer and Phil Poronnik

A TR(I)P through the world of epithelial calcium and magnesium channels
Merlin Thomas
Walter Thomas University of Queensland
Peter Thorn University of Queensland
Anuwat Dinudom University of Sydney
Stefan Bröer Australian National University
Phil Poronnik University of Queensland

Regulation of trafficking of membrane transporters by intracellular signaling systems

Organiser: Anuwat Dinudom

Regulation of receptors and transporters by the Nedd4 family of ubiquitin ligases
Sharad Kumar Institute of Medical and Veterinary Science, South Australia

To be advised
Rob Parton University of Queensland

The physiological roles of sulfate transporters
Daniel Markovich University of Queensland

The strange origins of the Student's t-test

The centenary of the introduction of the Student's t-test may not be as auspicious an anniversary as some, but the Student distribution around which the t-test is based has had an impact on experimental design and sampling theory far in excess of the modest intentions of its originator, William Sealy Gosset (Fig. 1). In order to fully appreciate the impact of the Student's t-test on modern biostatistical analysis we must travel back over a century to assess the current statistical trends of the day.

At the onset of the 20th century statistical analysis was dominated by the concepts of populations and very large sample numbers, whose chief advocate was Karl Pearson. The central core of such analysis was the normal distribution, which was first derived by de Moivre in 1733 (de Moivre, 1738) to predict the outcome of games of chance, and later, based on the application of the distribution to astronomical analysis, expressed as a probability frequency distribution (equation 1) by Gauss:

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}\frac{(x-\mu)^2}{\sigma^2}} \quad (1)$$

where σ is the standard deviation, and μ is the mean. A large number of parameters/characteristics in biology are accurately described by a normal distribution (Fig. 2), which has the following characteristics:

- it is symmetrical about the centre, with this as the point containing the highest frequency;
- the mean, median and mode are the same;
- the inflexion of the curve is ± 1 standard deviation (SD) from the centre (mean);
- the tails asymptote towards zero;
- the means of large groups of samples (n > 120) from within a population described by a normal distribution, will also be normally distributed (note that this is not the case for smaller groups of samples, the catalyst that impelled Gosset to establish his 'Student's t' distribution).

Since biological parameters of populations are accurately described by a normal distribution, it follows that the properties of the normal distribution can be applied to these parameters. The key characteristic of a normal distribution is that the area under the curve, which equates to the proportion of data lying between two points, can be defined in terms of SDs relative to the mean. Thus 68% of the area is contained within ± 1 SD of the mean, 95% of the area is contained within ± 1.96 SD of the mean, and 99% of the area is contained within ± 2.56 SD of the mean (Fig. 2). This ability to accurately define the distribution of data relative to the SD led to the concept of confidence limits, where the probability that data will lie between distinct SD spans can be stated as a percentage. For example, there is a 95% probability that a data point for any normal distribution will lie between ± 1.96 SD of the mean. The normal distribution can also be used to make inferences about data from two sample groups. If the mean of one sample group lies between the 95% confidence limits of the other sample group, there is only a 5% chance that the two sample groups are not drawn from the same population. This is a key relationship, as we shall soon see.

Figure 1. William Sealy Gosset (1876–1937), pictured around 1908.

It is at this point that William Sealy Gosset enters the picture. Born in Canterbury in 1876, Gosset was educated at Winchester and Oxford, where he obtained a first in chemistry in 1897 and a first in mathematics in 1899. He was hired by the Guinness brewery in Dublin, in whose employ he spent the remainder of life, mainly at St James Gate in Dublin, and for the final 2 years at Park Royal, London. Gosset's academic background may seem at odds with his employment as a brewer, but Guinness realized around this time that in order to maintain its dominant market share as the biggest brewer in Ireland, it would have to introduce brewing on a

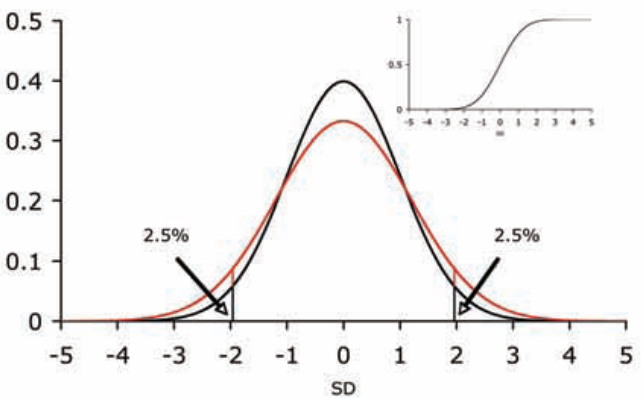


Figure 2 The normal and t distribution. The black line indicates a normal distribution with a mean of 0 and a SD of 1. The combined areas under the normal distribution bordered by the vertical black lines at ± 1.96 SD from the mean account for 5% of the area under the curve. The red line illustrates a t distribution, which is smaller and flatter than the normal distribution. An extension of the lines at ± 1.96 SD from the mean, meet the t distribution (red lines) encloses an area of greater than 5% of the area under the curve. Inset illustrates the cumulative distribution function for the normal distribution illustrated.

carefully controlled industrial scale. Such a venture would require rigorous quality control; hence the requirement for university trained chemists and statisticians. As any amateur brewer will attest, the brewing of beer has an element of the unknown, with success being not only dependent on the correct procedure, but also an element of luck! It was this reliance on luck for a successful product that Guinness sought to eliminate by scientific procedure. Beer, of course, is a combination of natural products; malted barley, hops and yeast, all mixed with water. These natural products share an inherent variability common to all agricultural products, whose quality is dependent not only upon crop variety, but also on climate, soil conditions, etc. Gosset's task as Apprentice Brewer was not only to assess the quality of these products, but also to do so in a cost effective manner. This necessitated using experiments with small sample numbers to draw conclusions that could be applied to the large scale brewing process. However, Gosset discovered that in using small samples the distribution of the means deviated from the normal distribution. He therefore could not use conventional statistical methods based upon a normal distribution to draw his conclusions.

In 1904 Gosset published an internal report entitled *The application of the 'Law of Error' to the work of the brewery*, where he described how '*the greater the number of observations of which means are taken, the smaller the (probable) error*'. Gosset also noted how, compared to a normal distribution, '*the curve which represents their frequency of error becomes taller and narrower*' as sample size decreases (Fig. 2, black line). The Guinness management realized the potential cost savings impact of the study and suggested Gosset consult with a professional mathematician.

Gosset therefore wrote to Karl Pearson at UCL, and they met on 12 July 1905 while Gosset was on holiday in England. This meeting led

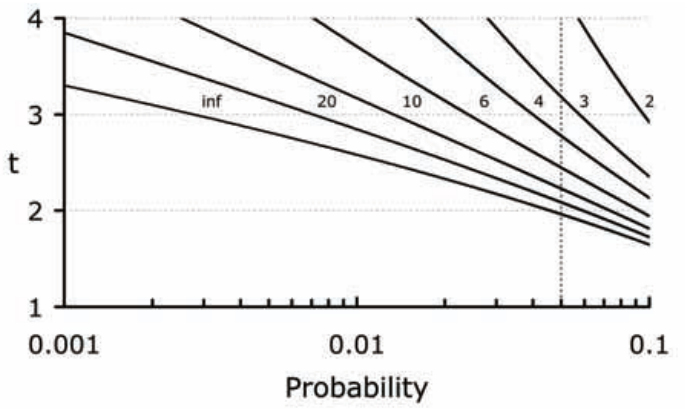


Figure 3. The value of t relative to the probability for an increasing value of n. At p = 0.05 (vertical dotted line) note how the value of t increases as the value of n decreases.

to an invitation for Gossett to visit Pearson's department at UCL in 1906/07 for a year, where he worked on his small samples problem. In 1908 Gosset published the fruit of his labours in a paper entitled *The probable error of a mean* in the journal *Biometrica* (Student, 1908), of which Pearson was Editor. However, Guinness had a policy of not publishing company data, and allowed Gosset to publish his observations on the strict understanding that he did so anonymously, and did not use any of the company's data. Gosset complied and published under the pseudonym 'Student' – the name under which he would publish 19 of his 21 publications. The name Student apparently came from the cover of a notebook Gosset used at the time – *The Student's Science Notebook* (Ziliak, 2008).

In his classic paper Gosset states that '*any series of experiments is only of value is so far as it enables us to form a judgment as to the statistical content of the population to which the experiment belongs*.' Or, stated another way – having n observations Gosset wanted to know within what limits the mean of the sampled *population* lay. In the paper Gosset partially derives the distribution of the error (termed z) and gives values of z from n = 4 to 10. This table is expressed as a cumulative distribution function (Fig. 2, inset) relative to n and z. The calculations required to generate the table of z values were very labour-intensive and took Gosset about 6 months to compute on a mechanical calculator, bringing to mind an equivalent labour carried out by Andrew Huxley in the mathematical reconstruction of the squid axon action potential (Hodgkin & Huxley, 1952). Gosset concluded the paper with several examples in which he computed the odds of a variety of scenarios occurring. To do this he simply divided the difference of the means by the standard deviation to calculate z, and then looked up the tables at the appropriate level of n. The cumulative distribution function was then converted to odds. The higher the value of z, then the greater the likelihood that the conclusions drawn from the test were correct. An essential component of the Student distribution is that, as the value of n decreases, so does the cumulative distribution function at the same value of z. Or, as we shall soon see, according to Fisher's argument the smaller the value of n the greater the value of t at the same probability (Fig. 3). This translated the familiar experimental scenario where the smaller the n value, the greater the difference between the two samples required in order to achieve any particular level of significance (Fig. 4). Such phrases as '*and in practical life such a high probability is in most matters considered a certainty*', '*but would occasion no surprise if the results were reversed by further experiments*' and '*would correspondingly moderate the certainty of his conclusion*' (Student,

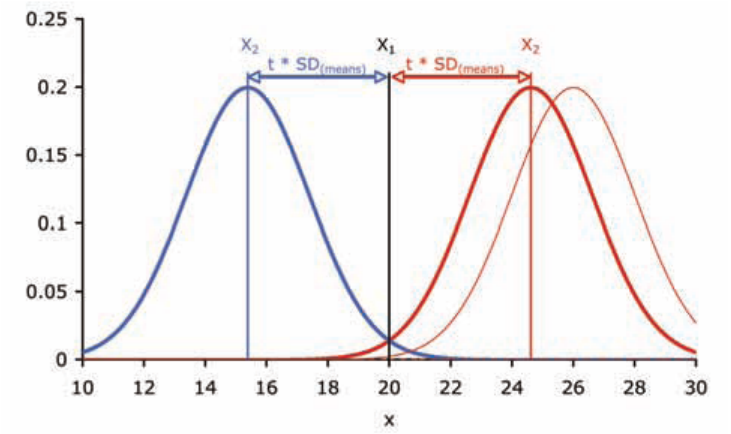


Figure 4. Graphical illustration of confidence limits and determination of significance between two groups. The mean of Group 1 is 20 (X_1), and the data have a SD of 2, and df of 8, with a resulting t value of 2.308. Thus the upper and lower 95 % confidence limits, respectively, are marked by the vertical red and blue lines at [20 – (2 * 2.308)] 15.384 and [20 + (2 * 2.308)] 24.384, respectively. If a second group of data have a mean value (X_2) of between 15.384 and 24.384, then this group of data are considered belonging to the same population as Group 1, as indicated by the normal distribution in thick red and blue lines. However, if the mean of Group 2 lies outside this confidence interval e.g. the thin red line normal distribution, then the group means are considered to be from different populations with a 95% degree of confidence.

1908), indicate the importance that Gosset put on the intuition of the individual experimenter or statistician in determining the meaning of the result. Gosset continued to use his table of z distribution in the course of his work, but otherwise it was ignored.

In 1912 Gosset communicated with a young statistician, Ronald Fisher, who would have an enormous impact on the acceptance of Student's distribution in day-to-day statistical analysis. Fisher is known today as one of the founding fathers of modern biostatistics, and he was not slow to appreciate Gosset's contribution. In 1917 Gosset published an extended table of z distribution for n = 2 to 30, stating of the table of z values in his 1908 paper '*I stopped at n = 4 because I had not realized that anyone would be foolish enough to work with probable errors deduced from a smaller number of observations*' (Student, 1917). Some years later In 1925 Fisher published a paper in which he fully derived the values of Student's distribution, his final distribution being equivalent to the form given by Gosset in 1908, and clearly showing it as a transformed normal distribution (Fisher, 1925). In this seminal paper Fisher also provided a worked example with two groups of unequal sample number. Fisher changed the nomenclature of the distribution from z, as it appeared in Gosset's original paper, to t, and changed the distribution from n to (n – 1) or degrees of freedom (df). On this amendment Gosset commented thus: '*When you only have quite small numbers, I think the formula we used (incorporating n – 1) is better, but if n be greater than 10 the difference is too small to be worth the extra trouble*' (Pearson, 1939). Pearson was skeptical, stating his contention that the number of samples should be large enough that n – 1 is indistinguishable from n. This reflected his continued resistance to the use of small sample numbers. However, Fisher must have exerted an influence at an early stage, as by 1917 Gosset was using (n – 1) in his extension of the table of z distributions (Student, 1917). Fisher also transformed the layout of Student's distribution to fit with his own agenda, namely to promote the use of probability as a determining factor in such calculations (Ziliak & McClosky, 2008). In Fisher's table the t value is expressed relative to p (probability) and df. Thus for a given df and desired probability the t value is located, and if this value is greater than the computed t value based on experimental data, then there is no significant difference in the data at that probability. This was certainly not how Gosset pictured his z distribution being used, but Fisher was an extremely eloquent and powerful advocate who rapidly came to dominate the field, and it is his form of the calculation that we use today (Rohlf & Sokal, 1995).

Gosset himself had no academic pretensions, and he comes across as a pragmatic man. He was dismissive about his mathematical ability, stating that the limits of his capabilities '*stopped at Maths, Mods [final examinations] at Oxford, consequently I have no faculty therein*' (Gosset, 1962). Gosset was clearly nobody's fool, but his mathematical skills were not on a par with Fisher or Pearson. That his derivation of t was incomplete and partly guessed bears out this point, but Fisher's fully derived t distribution of 1925 showed Gosset's intuition to be correct. Indeed Fisher comments '*any capable analyst could have shown him the demonstration he needed*'. Gosset's calculations frequently contained minor errors and he preferred to do his calculations on the backs of envelopes and scraps of paper (McMullen, 1939), an endearing amateurism only reinforced by comments such as '*In a similar tedious way we find*' during an extended derivation (Student, 1908). However, the t distribution allowed Gosset to proceed with his work for Guiness, and he was promoted to head experimental brewer and head of statistics, and finally in 1935 promoted to Head Brewer, a position he held until his death 2 years later.

This is a brief history of the introduction of Student's t distribution, but how is it applied in the Student's t–test? The first step in this calculation is to determine the value of t for the given df and level of probability which, for our purposes, we will take as 0.05 (5%). Given the t distribution we can then calculate

the confidence limits from the mean and SD of the sample groups (the t-test requires that both groups have the same variance and are normally distributed). Plotting these on a graph allows us to visually assess the data. If the mean of Group 2 falls outside of the upper and lower 95 % confidence limits (i.e. outside the confidence interval) of Group 1, then there is less than a 5% chance that the Group 2 data are from the same population as Group 1 (Fig. 4). It would be rather tedious to plot a graph of the data each time we wanted to compare two groups, but the graph can be reduced to a simple equation (equation 2).

$$t_s = \frac{|X_1 - X_2|}{SD_{(means)}} \quad (2)$$

where X_1 and X_2 are the means of the two groups, and the vertical lines are an indication to subtract the smaller value from the larger. In this equation t_s is calculated based on the experimental data. If t_s exceeds the t value for the appropriate df and probability (i.e $t_s > t$) then the two groups are different at that level of probability.

It should be fairly easy to see from Fig. 4 the logic of the equation. The greater the value of t_s the more likely the two groups are to be drawn from different populations, irrespective of df. The greater the difference between X_1 and X_2, or the smaller the SD (means) the greater the value of t_s. There are numerous spreadsheet examples of t-test calculations, which are worth doing once to see the workings of the equation, but are superfluous for day-to-day calculations since spreadsheets programmes such as Microsoft Excel have built in t-test functions, and the above equation only yields a t_s value, not the exact p values, which cannot easily be calculated.

In conclusion, physiologists (and many other experimental scientists) owe Gosset a debt of gratitude for rendering obsolete the reliance on large sample sizes to determine differences between groups of data. The t-distribution allows experimenters the freedom to use small sample sizes in the confidence that they are not compromising the validity of any conclusions drawn: indeed the Home Office policy of Reduction, Refinement and Replacement with regard to animal experiments would be impossible without the t-distribution.

That Gosset, surely the unsung hero of 20th century statistics, made such an enormous advance in the field of statistics is almost certainly due to his application of theory to solve practical problems. In a letter to Fisher regarding his t distributions Gosset lamented that *'you are the only man that's ever likely to use them'*. A browse through any issue of *The Journal of Physiology* will serve to illustrate the ubiquity of Student's t test in the life sciences, and demonstrate just how unaware Gosset was of the revolutionary impact his work would have on all fields of biology and beyond.

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CALENDAR OF EVENTS 2008

Beijing Joint Conference of Physiological Societies

October 19-22, 2008: Registration deadline July 15.
http://www.beijingphys2008.org/

The Australian Health and Medical Research Congress

Brisbane, 16th - 21st November 2008.
http://www.ahmrcongress.org.au/

Molecular Pharmacology of G Protein- Coupled Receptors,

5th International Meeting, Sydney, November 13-15, 2008.

These meetings attract outstanding national and international scientists; they are focussed and intimate (maximum of 200 attendees), emphasising novel concepts in GPCR pharmacology and drug discovery. The meeting provides a relaxed interface between students, postdoctoral fellows, academic and industrial scientists from around the globe that encourages interaction, collaboration and debate on the latest research in the field.

The program http://www.victorchang.edu.au/research/HomeandNews.cfm?cid=289 is looking exceptionally strong with acceptances from many of the major players in the field (Bouvier, von Zastrow, Coughlin, Sakmar, Ranganathan), including a showcase on the recent structural work of GPCRs by Kobilka, Schertler, Murakami/ Kouyama.
Registration is now open via the website.

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School of Molecular and Biomedical Science The University of Adelaide, Adelaide Australia.
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BIOLOGY OF LIPID METABOLSIM LABORATORY
More information: http://www.med.monash.edu.au/physiology/research/bolm.html
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For further information contact: A/Prof Matthew Watt, matthew.watt@med.monash.edu.au

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PhD opportunities currently exist in our internationally-recognised research programmes in the areas of Circulation, Integrative Physiology & Inflammation, Cellular & Molecular Neuroscience, and Membrane & Ion Transport.
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Positions and Scholarships continued

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The closing date for nominations is the 30th September, 2008.
Contact: AuPS secretary, Prof. Joe Lynch - secretary@aups.org.au

Senior Lecturer and Associate Professor in Neuroscience
Applications are called for two (continuing) academic positions in neuroscience, as part of the establishment staff for theTranslational Neuroscience Facility,
School of Medical Sciences, University of New South Wales (UNSW), Kensington Campus, Sydney, Australia.

Enquiries; Professor Gary Housley,
Head of Physiology, UNSW; email: g.housley@unsw.edu.au .
Applications should be lodged via UNSW employment, closing date 31st October, 2008.
http://www.hr.unsw.edu.au/services/recruitment/newjobaca.html

Meetings in 2009

Abstract submission for IUPS 2009 in Kyoto started on Sept 1st, 2008,
Invitation for Travel Grant Application for IUPS 2009 in Kyoto
Application for Young Investigators' Travel Grants are now open.
For more information please visit: http://www.iups2009.com
Send the application to: Travel Grant Committee
Secretariat of IUPS 2009
c/o Japan Convention Services, Inc.
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Tokyo 100-0013, Japan
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In order to apply, you must:

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