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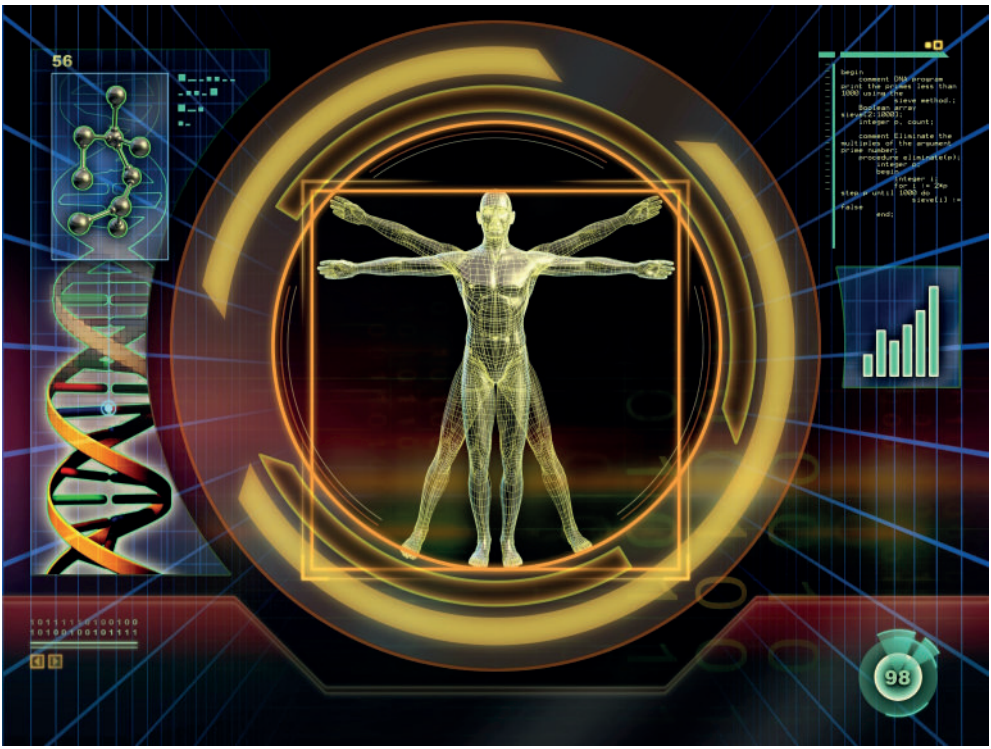
ADELPHI GENETICS FORUM

exploring heredity and society

Adelphi Review



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Adelphi Genetics Forum, 19 Northfields Prospect, London, SW18 1PE

Tel: 020 8874 7257 www.adelphigenetics.org

General Secretary: Mrs Betty Nixon

executiveoffice@adelphigenetics.org

Review Editor: Mr Robert Johnston

Charity No: 209258

EDITORIAL

It has been a long and wet winter since last October's Annual Conference but plans are already finalised for this year's event. **Helen Middleton-Price**, **Shirley Hodgson** and **Anneke Lucassen** have put together a terrific programme regarding how genomics has evolved since the publication of the completed Human Genome Project 20 years ago. Details can be found on page 20. Meanwhile in June, we are running our fifth conference for secondary teachers in Manchester and most places have now gone so don't delay if you're considering attending.

Andrew Read has produced another of his outstanding book reviews on page 12. This one considers Greg Radick's latest volume on the struggle between the Mendelians and the biometricians in the early 20th century. It certainly looks like it's worth a read.

We also have reports from two conferences that the Adelphi Genetics Forum has recently sponsored. along with information on how to apply for a grant to help with the running of your events.

Finally, I was so sorry to hear of the passing of **Professor David Galton** who was, for many years, an Officer and Trustee of the Galton Institute. We served on committees together and I always valued his wise contributions and kind words. You can find a tribute to him by Dian Donnai on page 16.

Robert Johnston

My Life in Genetics

An Interview with Dr George Burghel
Trustee of the Adelphi Genetics Forum

George Burghel

Tell us a little about your early years and interests

I grew up in Jordan in the Middle East. During my school years, my main interest was sports, especially long-distance running. I was also interested in science, fruit trees and classical Arabic poetry. Years later, I am still a runner (at a much-reduced speed) and a scientist with a huge appetite for fruits.

What first appealed to you about genetics?
As a very active child, I struggled at sitting still at school until I got an inspiring biology teacher who captured my attention. In year 11 we had a lesson about the central dogma of biology and the flow of information from DNA to RNA to protein. That concept was extremely fascinating to me and soon after that I started reading about genetics and twin studies which then put me on a one way road to a lifelong love and interest in DNA and genetics.

I took biology and human biology in my A-levels and was looking for a science/biology course at university. Towards the end of my school years, Jordan University of Science and Technology announced that they will be opening a new 4 year course, the first of its kind in our region: 'Biotechnology and Genetic Engineering' so I applied and joined the first cohort. Towards the end of my degree course the Human Genome Project was published and so was timely again for me to join a genetics lab in Jordan.

What is your main area of interest?
My main interest is cancer genetics. We do lots of tests within this field with direct impact on patient care at many levels. These include risk assessment, prevention and stratified care and treatment. One particular area of interest for me is circulating tumour DNA or liquid biopsies. This involves studying the DNA released from tumour cells into the blood instead of a tumour biopsy. This area is rapidly growing in clinical cancer genomics as it allows us to test patients who do not have an accessible tumour, or are too unwell for a biopsy to be taken. It also has the potential to allow very early detection and also to monitor treatment response.

Who has had the greatest influence on your work?

I was fortunate enough to have many positive influencers on my work, starting from my biology teacher at school, university lecturers and excellent supervisors in my post graduate studies. The person with the greatest and most recent influence is Dr Andrew Wallace who was the scientific lead for the cancer team in Manchester for many years and was the scientific director of our genomics hub before recently retiring. Andrew is the one of the most intelligent people I ever met in my life. He had a great vision for our team and was always approachable. Importantly, he was humble and always kept his cool even when under lots of pressure. He is very much missed by the cancer team in Manchester.

What role do you think the Adelphi Genetics Forum should play in promoting the subject?

I think the Adelphi Genetics Forum is amazing and one of the ways to help promote genetics more is by expanding into school outreach to introduce students to the amazing field of genetics as early as possible in their educational journey.

Tell us something about yourself that isn't widely known

When I was at school, I caught a live eagle which became my first and only pet. According to the vet, it had a minor injury in the wing and was lost and confused. We cared for it and it happily lived with us and was well fed. It even had the biggest room in the house. After a few weeks of amazing fun, the eagle seemed much better and stronger so we opened the window and let it fly away.

Previous contributors to the *My Life in Genetics* series:

Published in the ***Adelphi Review:***

Dr Helen Middleton-Price	**Issue 4**
Professor Nick Mascie-Taylor	**Issue 3**
Mr Robert Johnston	**Issue 2**
Dr Jess Buxton	**Issue 1**

Published in the ***Galton Review***:

Professor Nicholas Wood	**Issue 15**
Professor Dallas Swallow	**Issue 14**
Professor David Galton	**Issue 13**
Professor Andrew Read	**Issue 12**
Professor Veronica van Heyningen	**Issue 11**
Professor Dian Donnai	**Issue 10**
Professor Philippa Talmud	**Issue 9**

25th European Molecular Biology Laboratory PhD Symposium: Power of Many - Collective Behaviour across Scales

20-22 November 2023, Heidelberg

The focus of this year's EMBL PhD symposium taking place at EMBL Heidelberg was to unravel the vast range of effects arising from collective behaviour. Behaviour can be defined as the action of one entity in response to another. But, acting alone, the effect of singular units is limited. From molecular structures to cellular communication and complex ecosystems, the coordinated actions of functional units, to a common impulse, result in emergent behaviours. How does complexity arise and what ap-

proaches are currently being used to link individual actions to their ultimate consequence? As the cooperation between experts from across different disciplines is imperative, the symposium assembled and united a diverse array of researchers. We hoped to trigger fruitful discussions and exciting collaborations across disciplines to progress towards the lofty goal of advancing a holistic perspective on investigating biological systems.

This year's symposium organising committee was composed of over thirty first year PhD students from EMBL sites in Germany, France, Italy, Spain and the UK. We were thrilled to host over 160 participants from 25 different countries spread across all continents. The symposium provided a platform to both early-stage researchers and established group leaders from a wide range of disciplines to share their research in the form of talks and poster sessions.

Organising committee

Over the three days the conference was split into five sessions – Molecular Interactions, Cellular Behaviour, Multicellular Systems, Eco-Evolutionary Dynamics and Integration of Scales. Leading scientists in their field from different parts of the world along with international participants presented their cutting-edge research under these themes. Most sessions consisted of a mix of talks from keynote speakers, invited speakers and selected participants. In total we had the pleasure of listening to fifteen invited speaker talks and eight flash talks given by selected participants. A total of forty posters were also presented, of which nine were displayed virtually but with live interaction of the presenters.

The welcome address for the symposium was given by the Director General of EMBL **Edith Heard** who spoke about the importance of collective work and community in the advancement of science. The first session titled “Molecular Interactions” saw talks from **Fei Chen, Claudia Keller Valsecchi** and **Paola Scaffidi**. Fei Chen presented novel techniques that bridge single-cell genomics within space and time. Claudia Keller Valsecchi shared findings on the developmental impacts of gene dosage alterations, while Paola Scaffidi rounded out the session discussing the role of epigenomics in cancer promotion.

In the session “Cellular Behaviour”, **Verena Ruprecht** from CRG Barcelona gave the EMBO Young Investigator Lecture in which she spoke about mechanisms of cell and tissue plasticity in response to mechanical stress. This was followed by a talk given by **Samantha Stehbens** about how cell movement is regulated through physically challenging environments. **Elvan Böke** presented a second EMBO Young Investigator Lecture investigating the mechanisms by which oocytes evade ageing but later become susceptible with advanced maternal age. Finally, four stu-

dent flash talks were presented and then the poster session, where one half of the participants presented their posters, marked the end of the first day of the symposium.

Starting the “Multicellular Systems” session on the second day, **Gilles Laurent** presented the EMBO Keynote Lecture discussing the complexity and common principles of brain operations using reptiles and cuttlefish as examples. **Knut Drescher** and **Zev Gartner** then spoke about the dynamic mechanisms of bacteria in biofilms and swarms, and the self-organisation of cells into tissues respectively. This was followed by parallel sessions in which participants could attend tours of the EMBL core facilities and participate in seminars presented by either EMBO on open science, or **Anna Kreshuk** on AI for imaging analysis. The fourth session titled “Eco-Evolutionary Dynamics" began on Tuesday afternoon and included talks by **Jenny Tung, Rebecka Sepela** and **Elisabeth Ostrowski**. The topics included interplay between genomics and social behaviour in primates, microbial cues that guide octopus sensation, and cooperation and conflict in the social amoeba *Dictyostelium*. The second day ended with four more student flash talks, another poster session and a fun “scavenger hunt” around EMBL.

The final session, “Integration of Scales”, began on Wednesday morning and included **Bram van Dijk** who spoke about creating multi-level and multi-scale simulations of microbial evolution, and **Manolis Kellis** who covered a vast body of work that explored understanding genomes and disease mechanisms. **Ben Engel** presented the final EMBO Young Investigator Lecture on the relationship between organelle form and function with the use of cryo-ET. Following this session, a panel discussion on “Sustainable Science” helped us understand the problems surrounding sustainability in academia and research and the possible courses of action that could and should be investigated to achieve sustainabil-

ity. The panellists shared some personal anecdotes of their individualistic efforts of making their labs and scientific environments more sustainable. The panel included **Marta Rodriguez Martinez,** sustainability officer at EMBL Heidelberg, **Jeroen Dobbelaere**, sustainability manager at the Institute of Science and Technology, Austria, **Ben Engel** and **Soraya Zwahlen**, PhD student at EMBL and chair of Green EMBL Action Group. Lastly, **Barbara Treutlein** presented the final talk of the symposium with the EMBO Young Investigator Programme, discussing use of state-of the art single-cell transcriptomics methods to study cell fate in human tissues. The poster prize was awarded to **Jules van der Walt** from EMBL Grenoble (France).

The entire programme of the symposium along with details about the invited speakers can be found on the symposium website: https://phdsymposium.embl-community.io/main/ Finally, organising the symposium wouldn't have been possible without the generous support of the Adelphi Genetics Forum.

European Molecular Biology Laboratory

Grants for conferences and workshops

The Adelphi Genetics Forum makes awards of up to £1000 to help meet the cost of organising and running conferences or workshops on topics relevant to the Forum's aims. We will under special, exceptional circumstances increase funding up to a maximum of £2,000, if the request is well justified.

Full details of the grants can be found on our website at:
http://www.adelphigenetics.org/grants/grants-for-conferences-or-workshops/

The next deadline for grant submissions is 1st September, 2024

BOOK REVIEW

Disputed Inheritance - Gregory Radick University of Chicago Press 2023

To begin I must make a full disclosure: Greg Radick is an esteemed colleague and fellow Trustee of the Adelphi Genetics Forum. He is also Professor of the History and Philosophy of Science at Leeds University. But this is a review, not a puff-piece (though I should say that this is not a full academic review by a professional historian of science, more the reaction of an ordinary jobbing geneticist to an interesting and provocative book). The task of objectivity is made easier by the fact that this is not some easy-reading popularisation, but a serious scholarly book – 600 pages long, densely referenced and closely argued. It is intended as a corrective to common perceptions of genetics and its history.

The book has a hero, WFR Weldon, Professor of Zoology at Oxford University. At its core is a very detailed narrative of the often-acrimonious debates between Mendelians and biometricians concerning the nature of inheritance and variation that followed the renewed interest in Mendel's work in 1900. Weldon led the biometrical faction. As we all know, the Mendelians, led by the pugnacious Bateson, won. Maybe, thinks Radick, their opponents might have fared better had Weldon not died in 1906 with his definitive book unfinished. He wishes to reclaim Weldon for posterity and show how right he was.

Weldon was indeed right. In exhaustive experimental detail, he showed that the clear-cut dichotomous characters of the Mendelians were seldom seen in real-world breeding, and then only when all confounding influences of environment and ancestry (nowadays we would say the rest of the genome) were rigorously excluded. Perhaps counter-intuitively, Radick maintains that Weldon's core

beef with Bateson was not about dichotomies but about the nature and extent of dominance – a point I rather struggled with. But of course, Bateson was also right. The idea that an atomic theory of heredity could explain the inheritance of discontinuous characters was compelling. However, unfortunately many took the inherited 'atoms' to determine characters in a direct one-to-one way.

We are living with the consequences. The idea that there is a 'gene for' every character, and that they act in simple Mendelian ways to determine who we are, is widespread today. It has all the hallmarks of populism: simple, clear and wrong. And like other populist ideas, very persuasive provided you don't know too much about the subject. I'm not sure how many professionals fell for this. Clinical geneticists have a nice way of dealing with the Weldonian aspects: they divide characters in a rather fuzzy way into 'monogenic' and 'multifactorial', and they deal with the irregularities in 'monogenic' inheritance with the concepts of penetrance and expressivity (criticised in the book, but wrongly I think: penetrance is not a property of a gene, but of a *character*, given a genotype). But others, including enthusiasts for eugenics, took the exaggerated hereditarianism of 'gene for' Mendelism and ran with it. It was, as Radick points out, very useful to those who wished to maintain that inequalities in society were rooted in nature, and therefore should not be tampered with. They are still with us.

The final section of the book addresses how Mendelism became a core concept in biology, and sketches alternative ways of teaching elementary genetics. For me this was the least compelling part of the book. Radick ascribes the rapid acceptance of Mendelism to its combination of 'teachable principles, tractable problems and technological promise' - but goes on to point out that a more holistic Weldonian approach could have done the same. He seems to view 'Mendelism' as reliance on breeding ex-

periments, implying it was a spent force by around 1940. But post-1940 research in no way involved repudiation of breeding approaches, still less of Mendelism. It focussed on that key Mendelian concept, the gene - what genes are and how they work – and this required different methods. Clinical genetic research still depended on pedigrees right up to the era of exome sequencing. Maybe this is not Radick's own coinage but is embedded in the extensive literature he quotes, and with which I am not familiar – but I found it unconvincing. He makes a nice distinction between genes as character-makers ('the gene for') and genes as difference-makers ('the difference between two versions of this character can be due to the difference between two genotypes at this locus'). But I felt this was not always kept in mind, allowing justified criticism of the former to fall on the latter. And I wondered, might he be so keen to defend Weldon's position 120 years ago that he is wont to use his opponents' label as a term for everything that can be wrong in the teaching and application of genetics?

Certainly, there is a strong case to be made that conventional genetics teaching fosters a false and damaging belief in genetic determinism. The obvious place to start the fightback is in school. But Weldonising basic genetics teaching is not a simple task. Added to all its other attractions, the populist version is so easily examinable. I once bemused a meeting of Edexcel examiners by sketching an alternative genetics syllabus that would better relate to pupils' experience, in this era of DNA sequencing. But we all knew this was just entertainment. There is no way hard-pressed schoolteachers could take on a radically new syllabus, unsupported by course books and all the other infrastructure and, above all, far less easy to examine. Radick suggests that a simple first step would be always to add the words 'all else being equal' to demonstrations of the 3:1 etc ratios. Beyond that, norm-of-reaction graphs might replace Punnett squares as the central heuristic. And the failure of supposed human Mendelian characters (tongue

rolling, blue vs brown eyes etc) to perform as expected is surely a perfect tool for teaching Weldonian lessons.

If your job involves teaching genetics (or if you're just interested) you should take the time to read and digest this book. It presents a reasoned alternative to the standard narrative. It illuminates a lot of history that was much more complex than I had realized. It introduces the sympathetic figure of Weldon – I had supposed the biometricians were primarily Pearson and Galton. And it makes a case that, as Radick succinctly puts it, Mendel was not a Mendelian.

Andrew P Read
Trustee, Adelphi Genetics Forum

ADELPHI GENETICS FORUM

Fifth Teachers' Conference
Recent Advances in Genomics
Free conference for A-level science teachers in Manchester—28 June, 2024

Adelphi Genetics Forum is holding a conference *Recent Advances in Genetics* for A-level teachers at the Nowgen Centre, Grafton Street Manchester. Topics included in the programme:

- The principles of DNA sequencing and new DNA sequencing techniques
- Studying historical movements of populations using DNA
- Ethical issues of genomics in healthcare
- The potential applications of pharmacogenetics in the NHS
- Genomic testing for cancers
- Thoughts on the teaching of genetics in schools

OBITUARY

David Jeremy Galton

(born 2 May 1937, died 30 January 2024)

David Galton

Professor David Galton, who was a longstanding fellow and later Council officer of the Galton Institute, the predecessor organisation of the Adelphi Genetics Forum, has died aged 86.

After attending Highgate School in London, he studied Medicine at University College London gaining a BSc with first class honours in 1957 and MB, BS in1960.

After house jobs he went on to a fellowship to the National Institutes of Health in Bethesda Maryland DC which he much enjoyed, only returning because of the threat of conscription to the Vietnam war with his immigrant visa. After a further fellowship at the Hammersmith Hospital, he was appointed to the consultant

staff at St Bartholomew's Hospital and later to a professorship in the Department of Medicine, London University.

His clinical and research focus was on metabolic diseases particularly diabetes mellitus and the dyslipidemias and the genetic factors underlying these.

When asked what his most significant contribution to medicine had been, he replied ….'In 1983 we were one of the first to publish the use of a common single nucleotide polymorphisms (SNP) to identify susceptibility genes for hypertriglyceridemia. This followed from theoretical considerations by David Botstein and Walter Bodmer on the use of polymorphic DNA markers to construct a genetic linkage map for human DNA. We found a C3175>G transversion in the 3'UTR of the apoC3 gene at nucleotide 3175, where the rare S2 allele was associated with plasma levels of apolipoprotein C3, plasma levels of triglycerides and the occurrence of coronary atherosclerosis with the G allele'. He continued that not everyone believed the results due to small sample size but later GWAS studies supported their findings.

After retirement, he was a very active Fellow of the Galton Institute serving as Vice–President and later as Librarian. He was fascinated by the history of genetics and eugenics, perhaps suggested by his surname although he was no relation of Francis Galton. He published a number of books and articles in later life including 'Standing on the shoulders of Darwin and Mendel: their views on heredity'. CRC, Taylor & Francis 2018, **ISBN 9781138062177**

The Adelphi Genetics Forum extends their condolences to the family and friends of David.

Dian Donnai, Trustee Adelphi Genetics Forum

Research Students' Conference in Probability and Statistics 2023

10-14 September 2023 at the University of Sheffield

This was our 46th conference and since its inception in 1980, the RSC has developed into an annual conference at which PhD students from different institutions can convene, connect and share ideas. Postgraduate researchers working in fields relating to probability or statistics were invited to attend and present at the conference, which is organised and managed by fellow PhD students. This produces a sociable yet engaging environment, ideal for disseminating research to an international audience.

There were four invited keynote speakers, as well as forty student presentations. Presentations were punctuated by regular tea and coffee breaks, for delegates both to rest and to network. There were about sixty delegates in total, a number similar to RSC Nottingham held last year, although this year we chose to run it as an in-person rather than a hybrid conference.

On the first day we heard talks from two keynote speakers: firstly **Jennifer Visser-Rogers** from PHASTAR gave a great talk about public engagement and her experience with it; then **Nic Freeman** from the University of Sheffield spoke about mean curvature flow and the motion of hybrid zones (thin interfaces between populations that are genetically distinct, but still able to in-

terbreed.). We then had a poster and wine session which was very well attended, with lots of interesting discussions.

The following day, the contributed student presentations got underway, with fourteen sessions in total across the next two days. We heard talks from all areas of statistics and probability, including medical statistics, environmental statics, applied probability and Bayesian theory. Our third keynote speaker, **David Miller** from BioSS gave a very interesting talk about his research in statistical ecology and some great career advice! On Tuesday evening, after a BBQ for dinner, we ventured into the centre of Sheffield for an evening of bowling, pool and darts.

The student presentations continued on Wednesday 13th, along with our final keynote speaker, **Richard Wilkinson** from the University of Nottingham, who talked about computational statistics in the field of digital twins used in healthcare. The conference concluded with a gala dinner in Halifax Hall, during which the prizes for the best poster and three best presentations were announced.

The conference was attended by fifty nine students, from twenty seven different universities across the UK, Ireland and Italy. 39% of attendees were female. The organisers of RSC 2023 would like to thank the **Adelphi Genetics Forum** for their support of the conference. Without your contribution, some or all components of the conference would not have been possible.

James Salsbury

University of Sheffield

ADELPHI GENETICS FORUM

Conference 2024
The Royal Society - Wednesday, 16 October, 2024

Progress and challenges of implementing genomics into practice and society—the first 20 years

October 2024 marks 20 years since the publication of the completed sequence of the Human Genome Project (HGP) in *Nature*. The International Human Genome Sequencing Consortium's outstanding achievement gave rise to great hopes, with the expectation that it would enable 'researchers around the world to conduct even more precise studies of our genetic instruction book and how it influences health and disease'. How much of this prediction has been realised in the intervening years? This conference offers an opportunity to hear about some of the achievements, hurdles and failures of the intervening period from a variety of perspectives.

Speakers:

Anne-Ferguson Smith: *Epigenetic inheritance - models and mechanisms*
Bill Newman: *Implementing pharmacogenetics at scale in clinical practice*
Michael Parker: *The changing moral life of genetics and genomics since the Human Genome Project*
Andrew Read: *The Human Genome Project - 20 years on*
Fergus Shanahan: *No stool left unturned-why our microbiomes differ*
Steven Sturdy: *The fortunes of medical genomics: a quarter century of promise*
Clare Turnbull: *Genomics in population screening for cancer: opportunities, challenges and cautions*
Sarah Wynn: *The promise and challenges of genomics for patients and families affected by rare conditions*