Life Sciences Interface Doctoral Training Centre

Systems Biology Doctoral Training Centre

Key elements for success of Doctoral Training Centres

James Wakefield

Director, Life Sciences Interface DTC
University of Oxford

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- Introduction
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The need for cross-disciplinary training

"[There is a] need to drive up the supply of highly trained scientists and engineers, if the UK is to remain competitive in this century …Cross-disciplinary research must become an increasing priority in the inter-connected world of the future"

Ian Pearson, Minister of State for Science and Innovation (2007)

"As one of the world's leading pharmaceutical companies…it is vital that AstraZeneca recruit talented researchers to develop the next generation of medicines. However, with the rapid advances in drug discovery technology…the skills that we require for our business are also changing, with a need for cross-disciplinary experience in biology, chemistry, physics, applied mathematics, computer science and engineering"

Dr Andy Hargreaves, Director Advanced Science and Technology Lab, AZ

"If we (UK) wish to compete with the USA producing rounded, open-minded scientists, it is essential to teach a broad range of topics and encourage working with those from other disciplines. It would seem therefore that programmes like the DTC are essential"

4th Year LSI DTC Student, University of Oxford

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Graduate-level cross disciplinary training

- International reviews of subject areas repeatedly highlight that UK PhD are not “competitive”
  - Too narrow
  - Insufficient graduate level and generic skills training
  - UK graduates not competitive in the international job market in comparison to US and EU

- In 2002, EPSRC put out a call for proposals for Doctoral Training Centres at the Life Sciences Interface to:
  - provide training to allow those from a primarily physical sciences background to undertake research at the interface between Life, Medical and Physical sciences
  - Oxford was one of two initially funded later that year

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Oxford LSI DTC Students (2002 entry)

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Aims of Doctoral Training Centres

- To provide a supportive environment in which the students can make the transition from undergraduate learners to **cross disciplinary** graduate researchers

- For our students in Oxford, this involves provision of
  - basic background in biology, biochemistry, experimental techniques and biological physics
  - practical theoretical research skills in mathematical modelling, scientific computing, computer programming, statistical methods, and information engineering
  - extensive generic research skills training, focusing particularly on communication skills (presentations, writing, rhetoric, reading ethics, philosophy of science etc)

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Programme Structure

- 4 year programme
  - Just over 2 terms of intensive taught courses
  - 2 extended (12 week) research projects, one of which will (typically) lead onto the D.Phil project
  - 9 term doctoral research project working in one of the core research areas

- Strong support from the DTC throughout the 4 years

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A successful DTC?

- For the LSI DTC, EPSRC initially provided:
  - 10 Home/EU studentships per annum for five years
  - ~20% overhead to establish the Centre and the Training Programme
- This allowed us to lever support from the University (Division and Departments):
  - 4 additional studentships per annum
  - Ear-marked international scholarships (1-3 per annum)
  - Lecturers in appropriate areas to assist in teaching
- Programme renewed for a further 5 years in 2008
  - EPSRC cut support from 10 to 8 studentships per annum
- We still average cohorts of 16-20 students on LSI
- Net cost for training students per head is cheaper than normal DTA
- We have been awarded three additional DTCs

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Oxford DTC Programmes

- Life Sciences Interface (October 2002)
  - Biological Physics
  - Computational Biology
  - Mathematical Genetics and Bioinformatics
  - Medical Imaging and signals
- Systems Biology (October 2007)
  - Associated with the Oxford Centre for Integrative Systems Biology
- Systems Approaches to Biomedical Science (from October 2009)
  - Industrial Doctorate Centre
  - Partners include Astra Zeneca, GSK, Novartis, Pfizer, Roche, Microsoft, Fujitsu, GE Healthcare, Siemens, Philips and Celltech
- Next Generation Healthcare (from October 2009)
  - Brings together clinicians, medical imaging specialists, wet-lab researchers and industry
  - Run independently from the Institute for Biomedical Engineering (Hospital site)

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History in Numbers

- Total of 148 students have now entered the LSI and SysBio Programmes, 45 of whom have now successfully completed their D.Phils
- Approximately 25% of those who have graduated have gone into industry and 75% into academic research
- 90 of these students have been/are funded through the DTC grants, the rest are funded through a mixture of project, Departmental, University and international studentships and scholarships
- Students to date have been drawn from 29 different countries and every continent
- Total research council funding ~£24M
- Total non-research council ~£12.5M (excluding the new building)

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Do DTCs provide added value to a PhD?

"One of the things which has impressed me most whenever I have visited the DTC and met with your students is the esprit de corps that exists within and across each cohort of students. There is a vibrancy and excitement amongst each group about the possibilities that are being opened up to them by the multidisciplinary, collaborative approach to scientific research. This seems to be fostered by the immersive and supportive graduate training approach that you have adopted, and this in particular is something that I would like to promote right across the University."

Prof Keith Burnett,
Head of MPLS Division, University of Oxford (2007)

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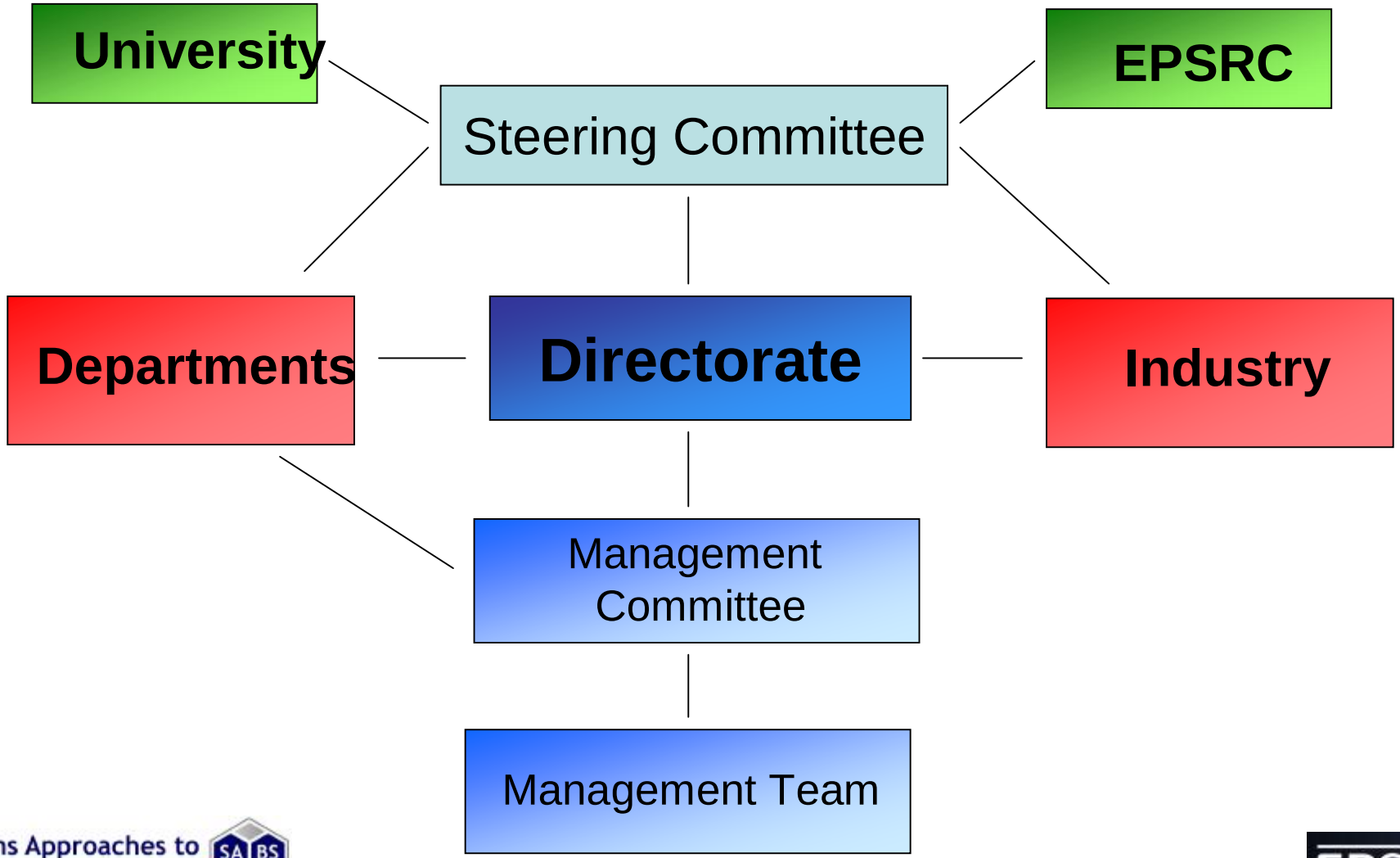
Management of the Oxford DTCs



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Teaching approach

"Many aspects of scientific research require a broad knowledge from many backgrounds and I felt the DTC course helped fill that gap" 4th yr student

- Intensive two- or three-week module structure allows students to obtain rapidly an excellent level of *core knowledge* and *conceptual understanding*
- Modules consist of:
  - directed reading - interactive lectures
  - problem solving classes - laboratory-based experimental work
  - programming practicals - workshops
  - journal clubs - student-led presentations
- All modules involve some aspect of formal assessment

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The DTC Learning Environment

"The DTC makes you feel like a proper scientist/researcher, equipping you with extra skills which other people don't have"

3rd year student

- Supportive, interactive, non-competitive
- Team-based, problem-based and application-oriented
- Multi-disciplinary
- Focusing on attainment of core skills and understanding
- Allows students to develop their own approaches to advanced learning

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Learning Environment

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Maintaining cohesion within and across cohorts

"Impressive how you manage to form a big "family" feeling" - 4th year student

- Students physically based together in the DTC for their first year
- Interactive and team-based approach promotes mutual respect and reliance
- Provides a network of expertise

- Research skills programme across cohorts
  - Comprehensive inter-year research seminar programme
  - Extensive generic skills training across all 4 years
- Encourage and organise regular sporting and social events
- Students feel like DTC students, even after integrating into Departments

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The student's perspective

- Creates a positive group dynamic within a supportive learning environment
- Provides a broad, individually-tailored training programme to each student
- Empowers students to determine their own research direction
- Allows a (very) informed decision based on experience
- Embeds transferable skills training within a coherent, training structure
- Creates a broad academic network amongst students and teachers
- Creates an atmosphere where there is a zest for scientific discovery

"Community of Scholars"

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The student's perspective

- *"Many aspects of scientific research require a broad knowledge from many backgrounds and I felt the DTC course helped fill that gap"*
- *"Knowledge of important papers and methodologies in my field meant I could hit the ground running"*
- *"The DTC makes you feel like a proper scientist/researcher, equipping you with extra skills which other people don't have"*
- *"After my first year I decided to switch to Medical Imaging, a decision I feel is one of the best I have made, and one which would have been impossible to make without being exposed to the DTC infrastructure"*
- *"I have really appreciated having a "ready-made" network of contacts with expertise across a range of subjects"*
- *"I feel that training in multiple areas makes me more employable"*
- ***"This really is the future of scientific research. To bring the community together instead of competing against each other for funding and publications"***

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The impact of DTCs on research in Oxford

- **Each of the research areas has expanded rapidly over the lifespan of the LSI DTC**
  - Over 25 permanent new UL posts have been created in research areas aligned to the DTC
- **Very strong output**
  - Over 200 student publications to date
  - 16 best presentation/poster prizes at international conferences
  - 6 Patents pending
- **Produces independent Researchers with broad and deep knowledge**
  - ability to work independently, to investigate and suggest new areas of research
  - gives broader understanding of research areas outside their own specialism
  - allows students to apply their existing knowledge to other areas
  - variety of backgrounds leads to diversity of knowledge and view points
- **Promotes Confidence/Self-Motivation**
  - the interactive nature of the teaching year exposes students to specialists early on in career
  - students expected to aid single-subject students once in research groups
- **Promotes collaboration where it would not have previously been possible**
  - Enhances own research and that of supervisor and research group

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The impact of DTCs on industrial and wider research communities

- Industrial Liaison Committee
  - Members from GE Healthcare, GSK, Siemens Molecular Imaging, Microsoft,Tessella, MedPharm, and Fujitsu
  - Provide advice and guidance on
    - Potential industrial collaborations
    - How we can make the programme relevant to industry's needs
    - Obtaining industrial sponsorship for studentships
  - Give seminars on industrial research, career opportunities in industry, and IP and legal issues

- Input will only increase with the advent of the IDC and NGHC Programmes

- Students exposed to leading national and international research and researchers through:
  - Associated conferences and workshops
  - Seminar series
  - Visitor programmes

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Dr Kieran Smallbone (2002)

algebraic number theory

$$= \left|N(\pi\sigma(\pi^{k-1}))\right| + 2(aA + 2bB) + 1$$

But $aA + 2bB > 0$ from lemma 4.3.1 as required.

If k is odd, $N\sigma(\pi^k)$ and $N(\pi\sigma(\pi^{k-1}))$ are both negative hence

$$\begin{aligned} \left|N\sigma(\pi^k)\right| &= N(\pi\sigma(\pi^{k-1}) - 1) = 2(aB + bA)^2 - (aA + 2bB - 1)^2 \\ &= \left|N(\pi\sigma(\pi^{k-1}))\right| + 2(aA + 2bB - 1) + 1 \end{aligned}$$

Again $aA + 2bB - 1 > 0$ from lemma 4.3.1.

As a simple corollary, if $\pi \in \mathcal{P} - \{\tau\}$ then $\left|N(\frac{\sigma(\tau^k)}{\pi^k})\right| > 1$, and hence $\mathcal{P}_0 = \mathcal{P}$ -

thus $\mathcal{J} = \{\eta \in \mathcal{O}_2 \mid \eta \text{ odd}\}$ as claimed in section 4.2.

Lemma 4.3.5. *Let $\mu \in \mathcal{O}_2^*$ be an odd integer ie $(\mu, \tau) = 1$. Then*

$$\sum_{\delta^* | \mu} |N\delta^*| \leq |N\sigma(\mu)|$$

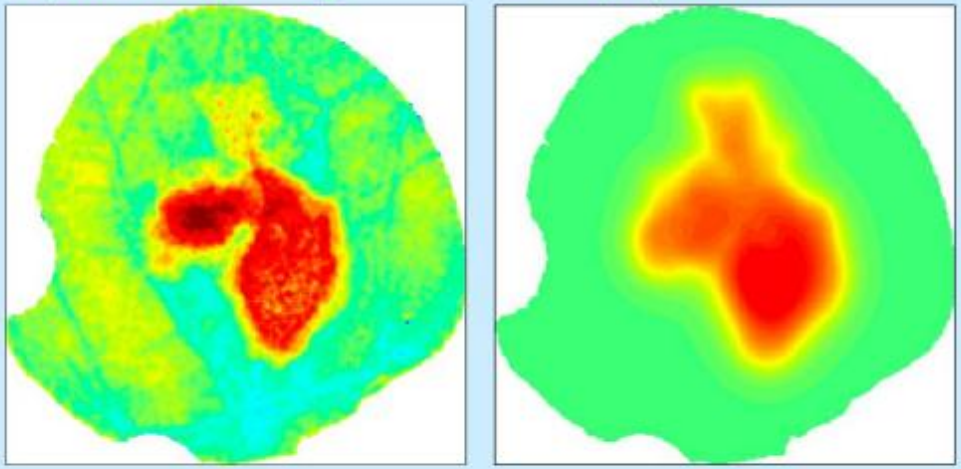
with equality iff μ is square-free and its prime factors $\pi \in \mathcal{P}$ have $\mathrm{Re}\,\pi = 1$

Proof. By induction on the number of prime factors of μ. Suppose first μ is a

pH image analysis

Experimental pH image

Model pH profile



: key clinical parameters

Now a Lecturer at Manchester Centre for Integrative Systems Biology

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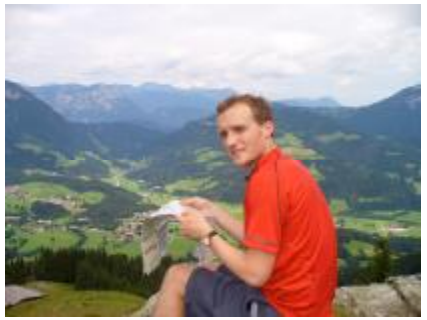
Dr Martin Bishop (2003)



Generating the 'Next Generation of Computational Cardiac Models'

Developing the pipeline to generate anatomically complex 3D computational ventricular models from high resolution (25 micrometer) MR data.

Now holds a Henry Wellcome Research Fellowship

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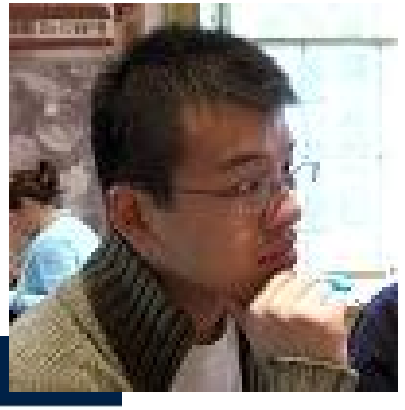
Dr Chris Yau (2004)



DEPARTMENT OF STATISTICS
UNIVERSITY OF OXFORD

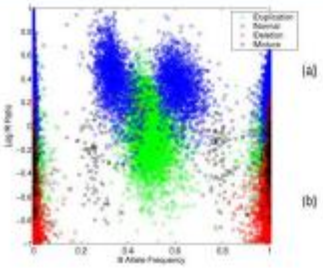
UNIVERSITY OF OXFORD

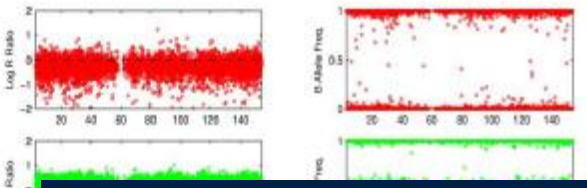
Identifying copy number alterations and loss of heterozygosity events in heterogeneous tumour samples

Christopher Yau and Christopher C. Holmes

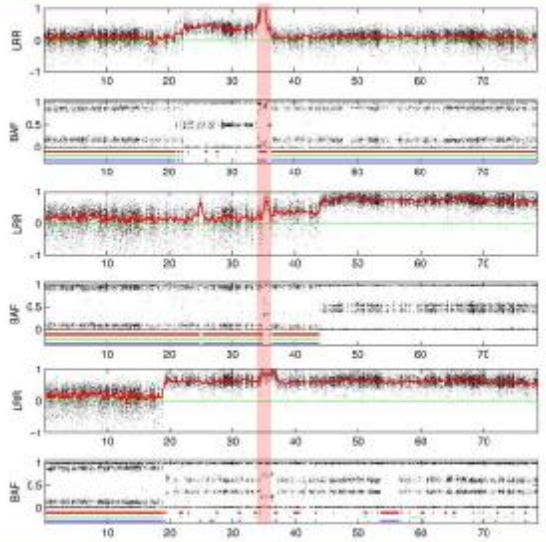
February 9, 2009

Real data





HER-2 Positive Breast Cancer



3x Breast tumour samples

HER-2 positive

Structurally diverse

Third individual shows trisomy-17 and will have an extra copy of HER-2 by virtue of the extra copy of chr17

What is the difference between HER-2 positivity due to gene amplification and polyploidy?

UNIVERSITY OF OXFORD

Now holds a MRC Training Fellowship in Biomedical informatics

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The future of cross disciplinary training

- The need for cross disciplinary training will only increase in the future
- Is a need to firmly embed training into Institutional structure
- Continued support from EPSRC over the next 5 years ensures medium-term viability
- The profile of the existing and new DTCs can be used to enhance visibility of cross disciplinary training within Departments currently not involved
- Long term embedding of a cross disciplinary training culture requires a concerted cross-Discipline and University-wide approach
- Implementation of “Graduate Schools” within Institutions is one possibility

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Thank you

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Prof David Gavaghan

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Ransom Khanye

Dr Charlotte Deane
Dr James Wakefield

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