



Doctoral Training Centre Integrative Systems Biology: from Molecule to Life (ISBML-Manchester)

This doctoral Training Centre trains students for a **Ph D in Systems Biology**. This is one of three Systems Biology training centres in the United Kingdom that have been funded by the EPSRC/BBSRC councils. It is open to EU students with masters in the biological, medical sciences or in the exact sciences or engineering. The 10 best students are funded by the EPSRC/BBSRC. This funding amounts to the annual University fee of 3.1 k£ for all EU(+UK) students plus a stipend of approx. 15.6 k£ per year for all EU students that have resided >3 years in the UK.

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Research:

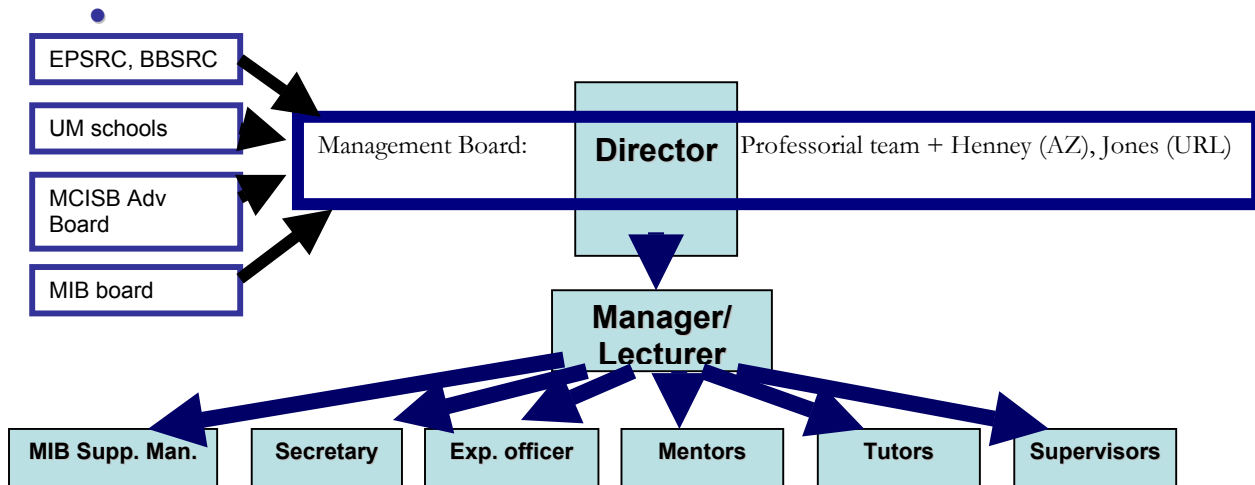
- 50+ research groups teaming up for systems biology from all relevant disciplines (from molecular and cell biology to mathematics and text mining)
- stimulated by a world class professorial team with all the required expertise (rated best SB expertise in Europe)
- already propelled by large Infrastructure grant BBSRC+ EPSRC (£ 6M) and by
- a multitude of SB related research grants; thereby:
 - clear focus ~everything is there (yeast up to silicon cell)
 - from that basis also other (mammalian SB; drugs, biotechnology, cosmetics)
- magnet for more and more groups worldwide
- UM: 2nd University for EPSRC grant support by number (4th by value). Equal top grant holder by value at BBSRC.
- Integrated partners in many worldwide SB consortia (IEcA, YSBN, RTKC, Silicon Cell)
- Connected (through the PI, who chairs it) to largest European national SB programme, Hepatosys
- Part of the only European Network of Excellence on Systems Biology (BioSim)

Teaching:

- An unconventional teaching program, tailor made for the essence of Systems Biology: integration
- Teaching program based on substantial existing experience of teaching Systems Biology (Amsterdam, [Gosau](#))
- Teaching program embedded in the environment of the excellent Doctoral Training Account tradition of UM
- Connected to European Systems Biology Training networks (Marie Curie NucSys)
- Connected to network of European Systems Biology Doctoral Training Centres

Management:

- Strict internal quality control of projects, students, coaching, science and postdoctoral follow-up (career)
- Clear definition of responsibilities
- Management Board including two members from industry



- **Environment:**
- MIB: a brand new building full of molecular, cell and systems biology
- A sense of novelty and making new things possible as a result of the merger of two research-intensive Universities
- Direct lines to relevant industries (AstraZeneca, Unilever, etc.); actual integration in their labs; Industry teaching parts of the course

Career:

- UM: voted top graduate employment University UK
- UM; Best careers service

Examples of projects:

~50 projects (3-page descriptions) proposed by all MCISB PIs, selected by Management Board, e.g.:

- **Vertical Genomics/Hierarchical regulation analysis in yeast** will study how the cell regulates a number of metabolic processes whilst it is responding to a shift in nutrient concentration (phosphate; parallel PDRA projects do carbon and nitrogen starvation). Changes in transcription rate, mRNA & protein concentration/phosphorylation/synthesis rate, V_{\max} of/flux through, the corresponding enzymes are measured quantitatively and analyzed using hierarchical regulation analysis. This will quantify the extent to which the process is regulated through transcription, protein stability, metabolically, etc. Then: silicon cell modelling, and other external challenges.
- **Antitumor drugs and EGF Systems Biology (AstraZeneca collaboration).** EGF applied to tissue culture cells, the phosphorylation of the MAP kinase proteins being followed quantitatively in time, is the core assay. Systems Biology laws concerning controls by kinases and phosphatases on the dynamics of phosphorylation (amplitude, duration, area under the curve, ...) will be tested and hopefully extended. EGF receptor mutation cells and drug-like molecules that act on the receptor and on the cascade will be studied. Hypothesis: drugs act best at sites to which control has shifted from the protein amplified by oncogenesis.
- **Skin ecosystems biology (collaboration with Unilever).** Microorganisms living on skin will be isolated and substituted by comparable model organisms in a laboratory model system. Their interactions will be determined by varying and measuring their abundances and studying the exometabolome. Metabolic activities in each organism will be followed and modelled. Regulation analysis will be performed for added substances relevant for skin.

- ***From metabolomics up: data driven hypothesis generation put into the context of the yeast model.*** Yeast cells will be challenged by a number of different perturbations (substrates, osmotic strength), both in batch and in chemostat. The responses will be different. Using metabolomics and transcriptomics data, the student will be asked to analyze the patterns and to see if he can come up with hypotheses of a limited 'space' of regulation.
- ***Systems Biology of translation in yeast.*** For protein synthesis in yeast, all components are available for an *in vitro* systems biology study. Concentrations will be varied the effects analyzed using and developing a mathematical model for translation.
- ***Yeast silicon cell: carbon and energy metabolism.*** Silicon cell type models are available for glycolysis. These will be extended to all major carbon and energy pathways, through modelling and experimental analysis. The student will examine possible 'metabolic apoptosis' states, e.g. when the pathways start at very low ATP/ADP ratio.
- ***The dynamics of NF κ B-mediated signal transduction.*** This will test the hypothesis that the time and space dependence of NF κ B signalling contains multidimensional functional information. Patterns of NF κ B signalling measured experimentally will be deconvoluted in space and time.