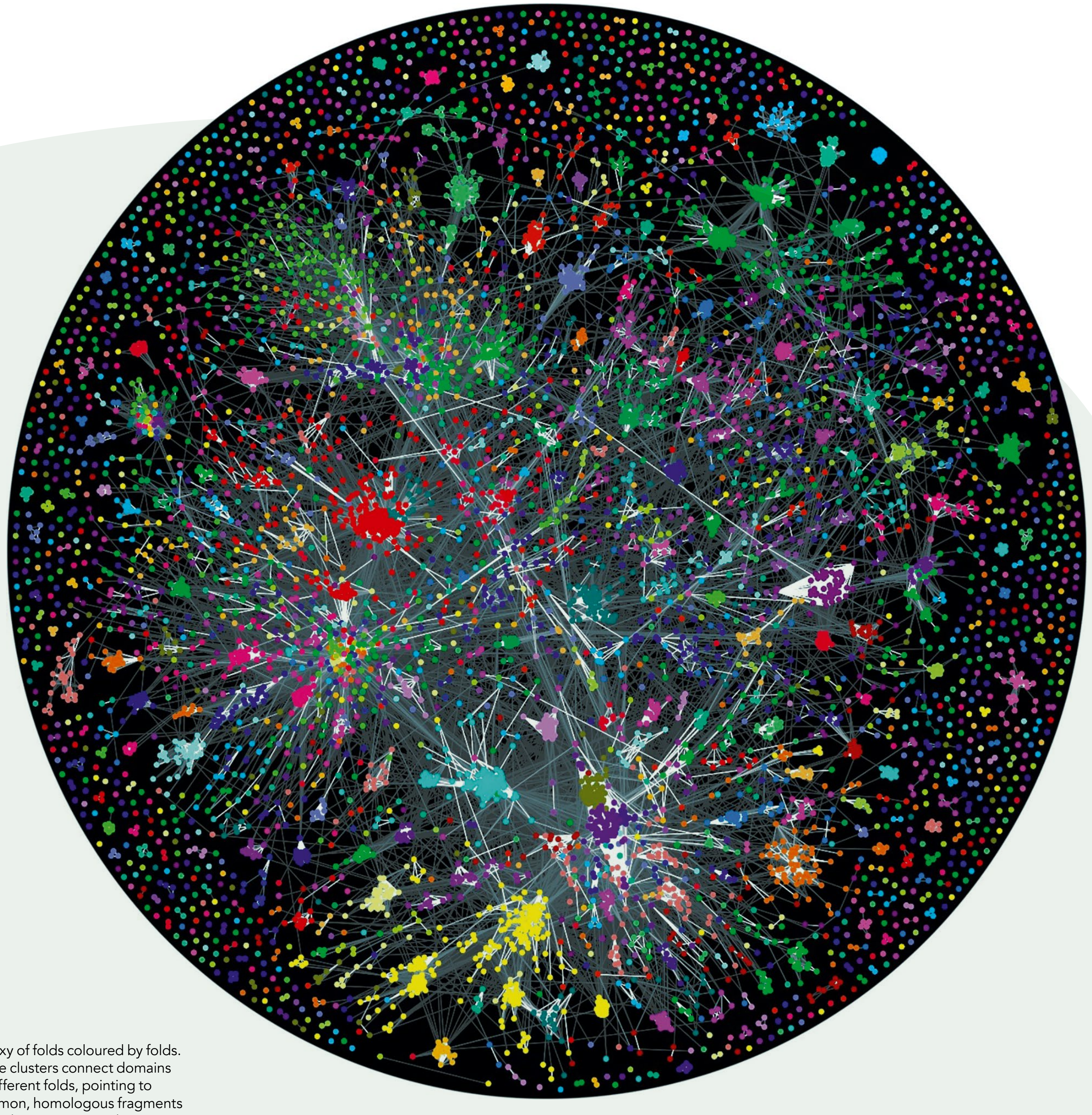
QBM: Taking molecular bioscience to the next level



Galaxy of folds coloured by folds. Some clusters connect domains of different folds, pointing to common, homologous fragments of similar sequence and structure. These might represent descendants of a set of ancient peptide modules, from which the first protein domains have been assembled.

Since its inception in 2012, the **Graduate School of Quantitative Bioscience Munich (QBM)** has been progressing successfully. Now in its fourth round of recruitment, the school receives over 200 applications a year from highly qualified young scientists from all over the world – a clear indication that there is a growing trend towards quantitative, system-oriented approaches in bioscience.

The Graduate School of Quantitative Biosciences Munich (QBM) was founded five years ago as part of the German Universities Excellence Initiative. Advocated by the German Federal Ministry of Education and Research and the German Research Foundation, this initiative aims to promote cutting-edge research by providing outstanding conditions for young scholars at universities and by encouraging deeper research collaboration between disciplines and institutions both nationally and internationally.

In light of this national effort, QBM was established in response to the increasing importance of quantitative and computational approaches among life sciences. Bringing together a wide range of disciplines – from biochemistry and medicine to bioinformatics, biophysics and applied mathematics – and uniting leading scientists from Ludwig-Maximilians University (LMU) Munich, Max-Planck Institute of Biochemistry and the Helmholtz Center Munich, QBM offers an integrated, interdisciplinary PhD programme that prepares young researchers for an emerging new era of quantitative, system-oriented bioscience.

"QBM students go through a rigorous training programme that familiarises them with the full breadth and depth of concepts and methods applied in current quantitative bioscience. The overall goal is to enable them to communicate effectively across disciplinary boundaries", explains Professor Ulrike Gaul, Speaker for QBM and Developmental Biologist at the Gene Center and Department of Biochemistry, LMU Munich.

WHY AN INTERDISCIPLINARY APPROACH IS NECESSARY

All too often, scientists with a background in molecular biology lack training in data analysis and statistics. This poses major methodological and conceptual challenges in the study of bio-molecular systems where the need for precise, high-resolution quantitation is a common theme. Increasingly central are mathematical and computational approaches, as well as mathematical modelling techniques that efficiently analyse high-dimensional data sets or capture biological processes in a mechanistically realistic manner. Indeed, advanced molecular biological research has intrinsically evolved into an interdisciplinary investigation that involves several disciplines, including biochemistry/structural biology, biophysics, bioinformatics, biostatistics, theoretical physics and molecular and organismal physics.

THE QBM PhD PROGRAMME

The QBM PhD programme consists of three main components designed to provide young scientists with the skills and resources to become scientifically multilingual. The first component is an interdisciplinary research project jointly supervised by two Principal Investigators (PIs) from different disciplines. The project is anchored in the student's primary field of training, but requires close interaction with a second discipline.

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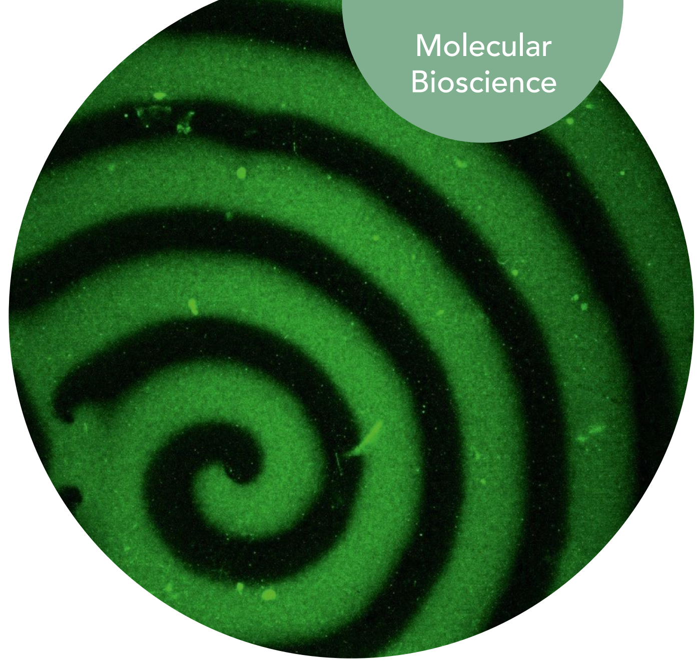


In *E. coli*, the Min proteins oscillate from pole-to-pole to determine the division site (Raskin and de Boer, PNAS, 1999). When reconstituted *in vitro* on a flat supported lipid bilayer in the presence of ATP, the Min proteins self-organise into dynamic patterns, such as surface waves and rotating spirals (Loose et. al., Science, 2008).

The second component is a substantial curriculum of formal coursework centred around a highly integrated interdisciplinary QBM Core course, the core element of the education programme. This intensive course addresses key problems in quantitative bioscience from multiple perspectives, to introduce and connect the entire spectrum of methods and concepts used in different disciplines.

Before the core curriculum of the QBM PhD Programme begins, students take 'primer courses', which aim to provide students with a basic background for what they will be learning later on. There are three of these primer courses, split into specific areas of scientific study, including: the Mathematical Methods and Physics Primer, the Bioinformatics/Statistics Primer and the Life Science Primer.

The first of these – the Mathematical Methods and Physics Primer – is a three-week long compact course that refreshes the mathematical background of life scientists. Students learn concepts in basic maths, through to higher maths – covering partial derivatives and mathematical applications to life science. Likewise, the physics aspect of this course introduces basic physics initially, before moving on to more complicated concepts – such as optics, atomic force microscopy and medical imaging.

Following this, students move on to the Bioinformatics/Statistics Primer course, with further introduction to data analysis tools. These include the Chi-squared test, z-test, t-test and ANOVA. Understanding the general mathematical concepts behind these tests helps the students to use them properly later on in the course. And, not only that, but the advantages and disadvantages of data analysis tools are discussed, helping students to understand which tools to use in specific scientific situations.

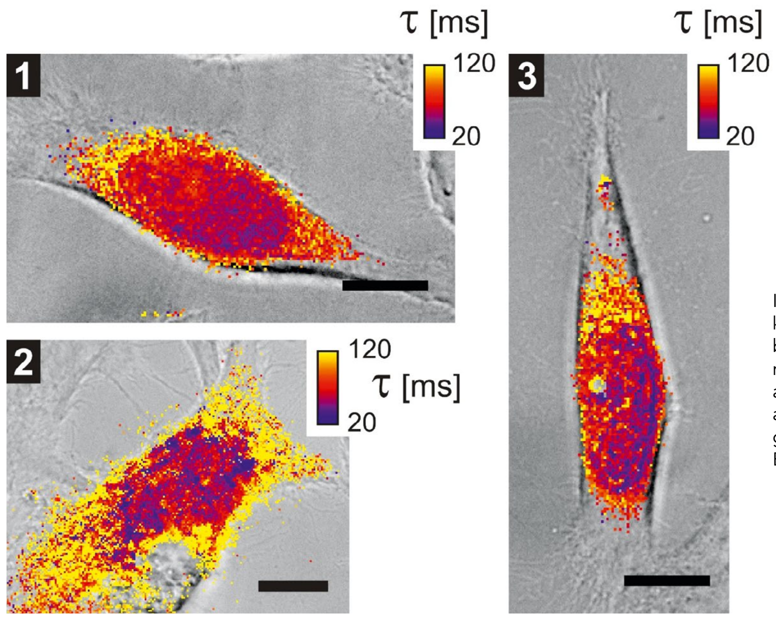
The third primer course is designed for students with a background in mathematics or physics, who have a limited knowledge or exposure to biological or biochemical concepts. For physicists, the principles of biochemistry and biology can be very different to those they are used to from learning physics. Therefore, a change of mindset is needed to appreciate how physics/mathematical processes can be applied to biological science. During this course, students learn the fundamental principles of cell biology, molecular biology, biochemistry and genetics.

Finally, the last component involves additional activities designed to enhance students' professional skills. Workshops on various topics, such as improving communication, team and leadership skills, project management, intercultural and gender awareness, are offered as electives.

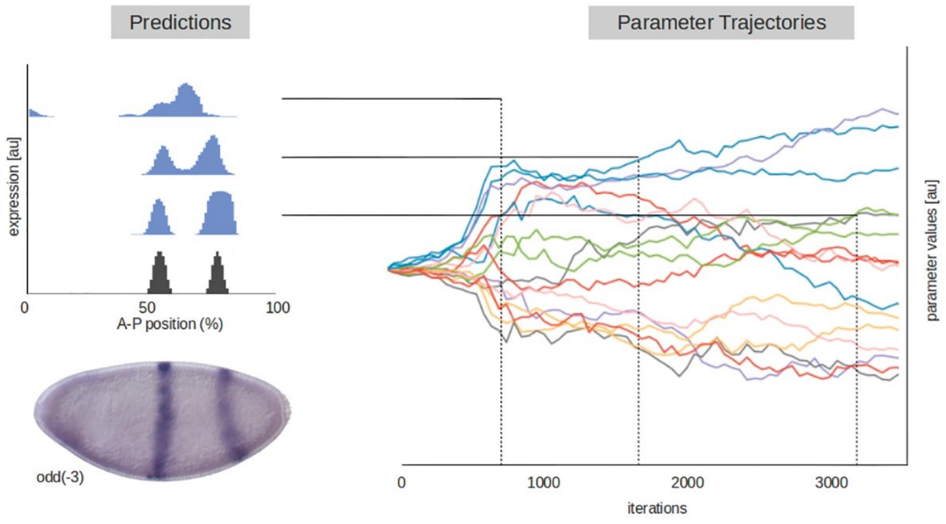
Successful execution of such a comprehensive programme requires a good balance of expertise. QBM has brought together 24 PIs from an array of disciplines, making sure there is an even mix of experimentalists and theorists with proven experience in working on biomedical problems, and in developing tools for quantitative analysis. While the overall scientific scope is the regulation of gene expression in all its facets, QBM aims to facilitate more holistic research efforts that characterise complex biological systems through quantitative models.

ORGANIC CROSS-COLLABORATION

From the beginning, QBM has encouraged interaction among the students and the participating labs. Joint coursework and research collaborations have increased scientific exchange and have fostered a strong team spirit among the students and labs. This has led to exciting results, high-impact publications and the hosting of numerous scientific events that feature leading international scientists. Moreover,



In living cells, the kinetics of DNA binding could be monitored with an all-optical lock-in approach by the group of Dieter Braun.



Three stages of parameter fitting for a model of gene regulation. The model predicts gene expression patterns in *Drosophila* embryos. By searching the parameter space, the model finds the correct parameters to predict the measured expression patterns.

QBM nicely complements the strategic initiatives and scientific goals of other LMU departments – particularly the Gene Center, the Department of Biochemistry and the newly established Research Center for Molecular Biosystems.

Due to its immediate success, QBM has strengthened the position of the LMU in this area, attracting highly qualified scientists from around the globe to LMU. The interdisciplinary nature of the research and the immediate financial support QBM receives is also helping to attract new faculty.

"Given the success of QBM and the clear need it fills in PhD-level training in the life sciences, we believe it is vital to preserve the programme beyond the Excellence Initiative," says Professor Gaul. "The programme has certainly proved to be an important educational component of a larger effort to strengthen quantitative system-oriented bioscience and integrate key aspects of life science research at the LMU."

Q&A

Crossing disciplinary boundaries is not an easy task. What are some of the challenges students and PIs face?

It is challenging to effectively communicate with scientists from adjacent disciplines, such that they can competently discuss methods and results in collaborative projects. Collaborations are necessary for most projects and take time to build. It may be more difficult to finish projects with multiple parties involved, and to come up with truly relevant interdisciplinary projects that still have a clear definition.

What are the advantages and disadvantages of having a 'holistic', interdisciplinary academic background?

The clear advantage of such a background is that it enables a scientist to think outside the box and to come up with truly novel solutions and creative approaches to scientific questions. Also, by keeping an open mind and being fluid in several scientific languages, scientists are enabled to develop well-rounded projects and ask the big questions in a cooperative manner. A disadvantage may be that by trying to consider all aspects from different disciplines, there is a certain risk of dissipating energy and losing the focus needed to successfully answer scientific questions.

Do the PIs need to have a comprehensive scientific background to be able to successfully guide students through a multi-disciplinary environment?

Some QBM principal investigators have the appropriate background to guide students through a multi-disciplinary environment. Others have to do it with their co-principal investigators, but in the thesis committee meetings all parties are present and there is a lively exchange between advisor, co-advisor and students.

With regards to career trajectories, do you have statistics that show where graduates have ended up?

Not yet – the first generation of students are in their fourth year, with the majority of them expecting to finish within the end of the year.

How does QBM compare to other interdisciplinary schools?

QBM is unique in the sense that it is not just an umbrella for diverse PhD projects. Rather, QBM offers a substantial programme of coursework that is designed to significantly broaden students' methodological and conceptual portfolio beyond their area of core competence. Students with a full training in a given field (biosciences, physics, mathematics) learn to collaborate on advanced scientific problems and simultaneously receive formal training in complementary areas. We thought long and hard about what to teach, and revised our curriculum in response to the feedback from our students. We now offer primer courses in statistics and bioinformatics, biophysics, and life science. Students learn the computing language 'R' in the first weeks of the primer courses and, in the Biophysics Primer, learn how to use MATLAB. Then, in the integrated Core course, they learn to approach key topics from different methodological angles. 90 minute lectures by PIs are followed by tutorials on data analysis. We start with protein structure, protein folding, superresolution microscopy, mass spectrometry and translation. Then we take a mathematics detour to study ordinary differential equations, with biological oscillators as a target, plus stochastics. After that, we introduce the world of -omics – feature extraction, high dimensional data analysis, transcriptional regulation, epigenetics, immunology, cancer, disease and disease models. We tackle embryonic pattern formation and partial differential equations, synthetic biology and, finally, evolution.

QBM students go through a rigorous training programme that familiarises them with the concepts and methods applied in current quantitative bioscience

Detail

RESEARCH OBJECTIVES

The Graduate School of Quantitative Biosciences Munich (QBM) represents a response to the dramatically increased importance of quantitative and computational approaches throughout the life sciences. Its aim is to prepare young researchers for this emerging era through a PhD training programme at the interface of experiment and quantitative theory.

FUNDING

Deutsche Forschungsgemeinschaft (DFG)

COLLABORATORS

Prof Dr Erwin Frey and the 23 other QBM Principal Investigators

BIO

QBM was set up in 2012 to bring together a range of diverse disciplines, including biochemistry, medicine, bioinformatics, experimental and theoretical biophysics, and applied mathematics. It also brings together leading scientists from Ludwig-Maximilians University, the Max-Planck Institute of Biochemistry and the Helmholtz Center Munich.

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