Three PhD student positions in systems biology

The Molecular Systems Biology group at the University of Groningen (Netherlands) has openings for enthusiastic and talented PhD students. The University of Groningen, located in the north of the Netherlands, enjoys an international reputation as one of the oldest and leading research universities in Europe (position at rank 80 worldwide) in the recent Times Higher Education Ranking.

The Molecular Systems Biology group aims at generating a systems-level understanding about the functioning of metabolism (Prof. Matthias Heinemann) and of growth regulation by TOR in budding yeast (Dr. Andreas Milias-Argeitis). Towards these goals, the group members combine classical and systems biology approaches exploiting latest state-of-the-art single cell technologies (such as microfluidics and optogenetics). Together, the members of the international and interdisciplinary team (i.e. PhD students and postdocs with backgrounds in biology, engineering, physics and mathematics) create an inspiring research atmosphere, on whose ground we recently published a number of high profile stories:

Dr. Andreas Milias-Argeitis:

Prof. Matthias Heinemann:

**Development and validation of a TORC1 biosensor for Saccharomyces cerevisiae**

**Description:** The Target of Rapamycin (TOR) is a kinase with high medical relevance. In budding yeast, TOR Complex 1 (TORC1) is the major regulator protein synthesis and the key coordinator of cell growth. A major roadblock in the field is the fact that we are still unable to measure TORC1 activity in single cells. In this project, we aim to develop a molecular FRET-based TORC1 biosensor that is suitable for real-time monitoring of TORC1 activity via microscopy. The sensor will be used to follow TORC1 activity dynamics upon nutrient switches. This project will be co-supervised with Prof. Kathrin Thedieck (University Medical Center Groningen)

**Tools and methods:** yeast genetic engineering, fluorescence microscopy, microfluidics

**Requirements:** Candidates should have a background in either biochemistry, structural biology or molecular biology. Familiarity with fluorescence microscopy is a plus. The candidates should have good command of English (oral and written) and possess excellent communication and collaboration skills.

**Starting time:** as soon as possible

**Advisor:** Dr. Milias-Argeitis, Prof. Kathrin Thedieck

**How does the metabolic oscillator influence the eukaryotic cell cycle?**

**Description:** We recently found that metabolism in yeast is an oscillator, which even seems to exert cell cycle control. The next challenge is now to identify the nature of this oscillator and to unravel the molecular connection to the cell cycle machinery. To address these challenges, we will use microfluidics, time-lapse microscopy, optogenetic tools and mathematical modeling to untangle the intricate interaction between these oscillators.

**Tools and methods:** microscopy, microfluidics, flow cytometry, optogenetics, modeling

**Requirements:** The project can largely be shaped by the applicant. Candidates can have a background in either biochemistry, molecular biology, biophysics or engineering. Ideally, candidates with only wet lab experience would also get into mathematical modeling, and candidates with only modeling/computational experience would also perform experiments. The candidates should have good command of English (oral and written) and possess good communication and excellent collaboration skills.

**Starting time:** as soon as possible

**Advisor:** Prof. M. Heinemann
A powerful new method for $^{13}$C metabolic flux analysis

**Description:** We recently developed a new method for flux balance analysis (FBA), with which we can make much better predictions than with classical FBA. We now would like to combine this new method with $^{13}$C labeling experiments to unravel intracellular metabolic fluxes with unprecedented accuracy. We hope that this new method will also allow to determine metabolic fluxes, when cells grow in complex medium, which is a major challenge in the field. Here, we will develop and use different computational tools and methods.

**Tools and methods:** stoichiometric models, flux balance analysis, $^{13}$C flux analysis

**Position requirements:** Candidates should have a background in either biotechnology, engineering, computer science or physics. Basic knowledge in metabolism is a plus. The candidates should have good command of English (oral and written) and possess excellent communication skills.

**Starting time:** as soon as possible. For this project, only students can be hired who have not lived in the Netherlands 12 months before taking up the appointment.

**Advisor:** Prof. M. Heinemann

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**Application**

Excellent and highly motivated candidates should send their application to Dr. Andreas Milias-Argeitis (a.milias.argeitis@rug.nl) or Prof. Matthias Heinemann (m.heinemann@rug.nl). The application should contain: (i) a CV, (ii) information about grades and other measures of success, (iii) two letters of recommendation (these can also be emailed directly), and (iv) a statement on how the candidate's prior experience/expertise could be connected to one of the above mentioned project. The position will be filled as soon as an excellent candidate is identified.

**Conditions of employment**

First, you will get a temporary position of one year with the perspective of prolongation for another three years. Before the end of the first year, an evaluation will take place as to the feasibility of successful completion of the PhD thesis within the next three years.
