Watching the Nanomachinery of the Nuclear Pore Complex at Work by High Speed-AFM

Main Proposer: Roderick Lim

Biozentrum and the Swiss Nanoscience Institute

University of Basel

roderick.lim@unibas.ch

Co-Proposer: Christoph Gerber

Department of Physics and the Swiss Nanoscience Institute

University of Basel

christoph.gerber@unibas.ch

Nuclear pore complexes (NPCs) form the sole passageways between the nucleus and cytoplasm in eukaryotic cells. The functional role of each ~100 nm-diameter NPC is to ensure that only specific molecules (i.e., cargo) gain access to the nucleus. To do so, the NPC *a priori* inhibits macromolecules above 40 kDa from traversing its channel. Presently, the NPC mechanism remains unresolved although it is likely based on biochemical recognition and not size exclusion *per se*. Exclusive access is given to specific cargoes that are accompanied by transport receptor proteins (i.e., karyopherins or Kaps) that interact with the NPC nanomachinery. These consist of ~200 intrinsically disordered proteins (i.e., resembling random coils; known as phenylalanine-glycine (FG)-repeat nucleoporins or FG Nups) that collectively form a barrier within the central NPC channel. Given that structural analysis (i.e., electron microscopy, X-ray diffraction, etc) remains formidable (due to their lack of structure), FG Nup studeis have been restricted to *in vitro* biophysical or biochemical analyses. Not surprisingly, inherent differences in experimental approach and length-scale have resulted in contrasting views on the selective barrier mechanism. In this work, we want to validate the underlying molecular mechanism of the NPC by obtaining a real time view of FG Nup dynamics and cargo translocation at the single NPC level *in situ.* **We therefore propose to apply high speed-AFM (HS-AFM) <u>as the only possible means</u> to watch the nanomachinery of the NPC at work.**

Prof. Roderick Lim

Biozentrum and the Swiss Nanoscience Institute, University of Basel
Klingelbergstrasse 70, CH-4056 Basel, Switzerland
Tel: +41 61 267-2083; Fax: +41 61 267-2109
roderick.lim@unibas.ch

Education

Ph.D., The National University of Singapore/Institute of Materials Research and Engineering (Singapore)
"*Solvation Forces in Confined Molecular Liquids"*, 2003.
B.Sc. in Applied Physics, The University of North Carolina at Chapel Hill, 1996.

Employment

2009 – pres.	Argovia Professor for Nanobiology (Tenure Track Asst. Prof.), Biozentrum and the Swiss Nanoscience Institute, University of Basel, Switzerland
2004 – 2008	PostDoc, Biozentrum and the Swiss Nanoscience Institute, University of Basel, Switzerland

Honors and awards

2008 Pierre-Gilles de Gennes Prize: "From Solid State to Biophysics"
2004 International Fellowship awarded by the Agency of Science, Technology and Research (Singapore)

Key Publications (in "**bold**" = corresponding author)

R.L. Schoch, L.E. Kapinos, **R.Y.H. Lim**, Nuclear Transport Receptor Binding Avidity Triggers a Non-Monotonic Collapse Transition in FG-Nucleoporin Molecular Brushes, ***PNAS***, 109 16911 (2012).

M. Plodinec, M. Loparic, C.A. Monnier, E.C. Obermann, R. Zanetti-Dallenbach, P. Oertle, J.T. Hyotyla, U. Aebi, M. Bentires-Alj, **R.Y.H. Lim** and C-A. Schoenenberger, The Nanomechanical Signature of Breast Cancer, ***Nature Nanotechnology***, (2012) DOI: 10.1038/NNANO.2012.167.

S. W. Kowalczyk, L. Kapinos, T. Magalhães, P. van Nies, **R. Y. H. Lim**, and **C. Dekker**, Single-Molecule Transport Across an Individual Biomimetic Nuclear Pore Complex, ***Nature Nanotechnology*** 6, 433 (2011).

J.T. Hyotyla, J. Deng, **R.Y.H. Lim**, Synthetic Protein Targeting by the Intrinsic Biorecognition Functionality of Poly(ethylene glycol) Using PEG Antibodies as Biohybrid Molecular Adaptors, ***ACS Nano*** 5, 5180 (2011).

R.Y.H. Lim, B. Fahrenkrog, J. Koser, K. Schwarz-Herion, J. Deng, and U. Aebi, Nanomechanical Basis of Selective Gating by the Nuclear Pore Complex, ***Science*** 318, 640 (2007).

R.Y.H. Lim, N.P. Huang, J. Koser, J. Deng, K.H.A. Lau, K. Schwarz-Herion, B. Fahrenkrog and U. Aebi, Flexible Phenylalanine-Glycine Nucleoporins as Entropic Barriers to Nucleocytoplasmic Transport, ***PNAS*** 103, 9512 (2006).

R. Lim and **S.J. O'Shea**, Solvation Forces in Branched Molecular Liquids, ***Phys Rev Lett*** 88, 246101 (2002).

Prof. Christoph Gerber

Christoph Gerber is the director for Scientific Communication at the Department of Physics, University of Basel.

For the past 30 years, his research has been focused on Nanoscale Science. He is a pioneer in Scanning Probe Microscopy, and he made major contributions to the invention of the Scanning Tunneling Microscope and the Atomic Force Microscope (AFM), he is also a co-inventor of Biochemical sensors based on AFM Technology.

He is the author and co-author of more than 160 scientific papers that have appeared in peer-reviewed journals and has been cited more than 23‘000 times in cross-disciplinary fields.

He belongs to the one hundred worldwide most cited researchers in Physical Sciences. He has given numerous plenary and invited talks at international conferences.

His work has been recognized with multiple honorary degrees and various awards and appeared in numerous articles in daily press and TV coverage.

He is a Fellow of the American Physical Society, a Fellow of the World Technology Network and a Fellow of the IOP Institute of Physics UK.

He serves on the advisory board of several nano institutes and has chaired and co-chaired various international conferences. His IP portfolio contains 37 patents and patent publications.

His current interests include

- Biochemical sensors based on AFM Technology
- Chemical surface identification on the nanometer scale with AFM
- Nanomechanics, nanorobotics, and molecular devices at the ultimate limits of measurement and fabrication
- Atomic Force microscopy research on insulators
- Single Spin Magnetic Resonance Force Microscopy (MRFM)
- Self-organization and self-assembly at the nanometer scale