

**Seminar Series of the
CENTRE FOR RESEARCH IN MOLECULAR MODELING**

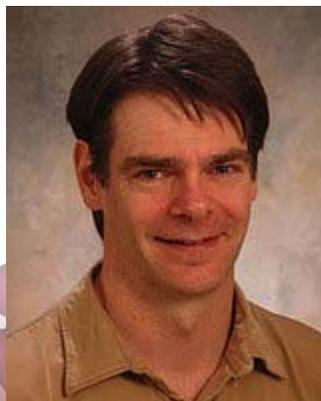
April 30th, 2010, 5:00 pm – Montefiore Club, 1195 Guy St.

***Computational study of the ligand-activated
glutamate receptor***

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Ligand-gated ion channels mediate information transfer at synapses. The binding of neurotransmitter molecules to the ligand-binding domains (LBDs) of these channels drives the opening of transmembrane pores, allowing the flow of select cations across the cell membrane. The ionotropic glutamate receptor ion channels (iGluRs) mediate excitatory responses at the vast majority of synapses in the brain and spinal cord. Our approach is to use equilibrium free energy computations based on detailed atomic models to elucidate the energetics that govern the allosteric mechanisms responsible for iGluR function. Ligand binding has been shown experimentally to proceed in two steps, in which rapid ligand docking is followed by slower domain closure. Understanding the energetics that govern these processes are critical to understanding the fundamental, microscopic basis for receptor activation. We compute the free energy of binding for ligands to iGluR2 using a novel methodology that rigorously accounts for the free energies of both docking and domain closure. The computations advance the understanding of the fundamental mechanisms by which dysfunction in iGluRs give rise to neurological disorders and will aid the design of novel iGluR ligands that can act as therapeutic agents.



Benoît Roux was born in the city of Montreal, Canada, in 1958. In 1981, he received a B.Sc. in Physics from the University of Montreal, followed by a M.Sc. in Biophysics in 1985 under the supervision of Remy Sauve. In 1990, he obtained a Ph.D. in Biophysics from Harvard University under the direction of Martin Karplus. In the last decade, he has held positions at the University of Montreal, and the Weill Medical College of Cornell University. Since 2005, he is Professor in the Department of Biochemistry and Molecular Biology at the University of Chicago with a joint appointment as Senior Computational Biologist at Argonne National Laboratory.