



#### AT A GLANCE

Founded: 2014

Program Directors: R. J. Dwayne Miller, Max Planck Institute for the Structure & Dynamics of Matter, and Oliver P. Ernst, University of Toronto

Fellows and advisors: 15

Institutions represented: 14, in 5 countries

Fields and subfields: biophysics; biochemistry and molecular biology; structural biology; genetics; neuroscience; basic medicine, including pathology, pharmacology and toxicology; analytic and organic chemistry; optics

Interaction meetings: 2; in Toronto, Canada and Martinsried, Germany

Relevant knowledge users: industry (e.g., pharmaceuticals, medical devices, surgical technologies, etc.)

# MOLECULAR ARCHITECTURE OF LIFE

**Seeks to untangle the details of the complex molecular processes that underlie all living systems, with implications for everything from our understanding of evolution to our ability to treat disease.**

The program in the Molecular Architecture of Life completed its first full term year in 2015/2016. During the year, the program increased its membership from ten to 15 researchers from Canada, the United States, Germany, the United Kingdom and Switzerland. Fellows launched five new collaborative projects within the group and with meeting guests.

The year's two program meetings were critical to assessing and validating that the technology is now in place to define a larger project for biology: making a molecular map of the cell. This project — comparable in scope and impact to the Human Genome Project — will require a massive international effort.

Even with the necessary techniques in place, the correlation of the data, its reduction to simple physical mechanisms of organization and the mathematical/theoretical modelling of networks that control living systems will require enormous human resources. The program in the Molecular Architecture of Life has identified and begun exploring key model systems to which these new technologies can be applied, in order to lay the groundwork for developing the molecular map of the cell. Moreover, fellows have begun to identify and engage with the leading international researchers, potential research partners and end users who will be critical to advancing this work. The program's next meeting, to be held in China in partnership with the Chinese Academy of Science, will begin this discussion in earnest as a first step toward determining the level of co-operation that can be achieved to reach this grand goal.

**Research**

- Transmission electron microscopy (TEM) had been assumed unamenable as a technique for imaging live cells, as it could cause electron-induced damage to the sample. This year, the research group of Program Co-Director and Senior Fellow **Dwayne Miller** (Max Planck Institute for the Structure & Dynamics of Matter) developed a new liquid sampling concept that permitted them to use TEM to successfully image DNA hybridization at the single molecule level. The work is a significant breakthrough that improves on the capabilities of super-resolution microscopy, which received a Nobel Prize in 2014.
- Program Co-Directors and Senior Fellows **Oliver Ernst** (University of Toronto) and **Dwayne Miller**, with other collaborators, discovered that the first molecular reaction in vision generation happens much faster than any previously known biological process, occurring at the very limits of what is theoretically possible in biological functions. The team also found that the vibrational motions of the molecules help direct the chemical reaction. These findings are important to elucidating the most critical details of how molecular receptors receive information precisely and relay it onward, in this case to our brains where we process images.
  - > Mueller C, Marx A, Epp SW, Zhong Y, Kuo A, Balo AR, Soman J, Schotte F, Lemke HT, Owen RL, Pai EF, Pearson AR, Olson JS, **Ernst OP, Miller RJD**. 2015. Fixed target matrix for femtosecond time-resolved and in situ serial micro-crystallography. *Struct Dyn*. 2(5): 054302.
  - > Johnson PJM, Halpin A, Morizumi T, Prokhorenko VI, **Ernst OP, Miller RJD**. 2015. Local vibrational coherences drive the primary photochemistry of vision. *Nature Chem*. 7: 980-986.
- Protein-ligand interactions are fundamental to almost all processes occurring in living organisms. New collaborations among program fellows, including **Krzysztof Palczewski** (Case Western Reserve University), **Wolfgang Baumeister** (Max Planck Institute for Biochemistry), **Dwayne Miller**, CIFAR Advisor **Daniel Müller** (ETH Zurich) and others, have brought together the know-how for sample preparation, data collection and analysis required to capture 'molecular movies' — extremely complex, billion-dollar experiments that will allow the team to explore and understand the otherwise inaccessible processes behind protein-ligand interactions.

**IdeasExchange**

- The technological developments arising from this program have the potential to transform how we understand and treat human diseases. One example is a new laser surgical method, developed by the Miller group, which is the first to eliminate the formation of scar tissue in the healing process. Discussions over the past year have identified several potential key partner/knowledge user groups, such as pharmaceutical and medical device companies, and round tables to engage these groups will begin in the coming year.

**Global Academy**

- The program engaged two postdoctoral fellows to serve as program meeting reporters and provide written summaries of each presentation after the meeting. Fellows committed to hosting a satellite meeting for postdocs and graduate students in the fellows' research groups, in conjunction with one of next year's program meetings. The satellite meeting will be organized by a group of senior trainees and will facilitate an overlap of participation in both events.

To learn more: <https://www.cifar.ca/research/molecular-architecture-of-life/>

The program in the Molecular Architecture of Life met at the Max Planck Institute of Biochemistry in Martinsried, Germany, in April 2016.

