

## MEETING REPORT

# Navigating the cell: how motors function *in vivo*

 Enrique M. De La Cruz<sup>1,\*</sup> and Erika L. F. Holzbaur<sup>2</sup>

## ABSTRACT

The Company of Biologists Workshop entitled ‘Navigating the Cell: How Motors Function *in vivo*’ was held in March 2014 at Wiston House in Steyning, West Sussex, UK. The meeting was an opportunity for a diverse group of experts in the biology and physics of cytoskeletal dynamics, and molecular motors to come together in a setting that promoted scientific interactions and the development of new collaborations. Here, we summarize the highlights of the meeting, one of which was the unique organizational principle that promoted cross-fertilization of ideas and approaches among the participants.

This meeting was organized around a very timely topic – how cytoskeletal polymer dynamics and the motor proteins that interact with the cellular cytoskeleton power movement. Decades of research on the biochemistry and biophysics of molecular motors, and the cytoskeleton has revealed a great deal about how these proteins work on the molecular scale. However, our knowledge falls far short of the goal of obtaining a mechanistic understanding of cytoskeletal and organelle dynamics in living cells. This gap remains because of the complexity of the intracellular environment where, for example, multiple types of motor protein bind to cargo and multiple systems of cytoskeletal filament interact. We also have much more to learn about the physical properties and the forces that govern intracellular dynamics at cellular length and time scales, and the emerging behavior of interacting systems.

‘Navigating the Cell’ was an exciting meeting designed to bring together a diverse group of investigators that are interested to fill the gaps in the current knowledge in this area. Meg Titus and Volodya Gelfand invited biochemists and geneticists, cell biologists and soft condensed matter physicists, mathematicians and biophysicists to spend four days discussing issues at the forefront of research in this field. The meeting was divided into five scientific sessions, comprised a junior investigator poster session, and plenty of time was allotted for discussion throughout the day.

The workshop could easily have been subtitled ‘cytoskeletal dynamics from A to Z’ or, at least, from Bielska to Zala, because Meg and Volodya used a novel organizational strategy to arrange the order of speakers, based almost entirely on alphabetical order. This acted as a randomizing element: for example, a physicist’s talk was followed by one from a geneticist, and a biochemically oriented presentation was followed by a more biophysical talk. The result was dynamic and exciting, as commonalities in the questions being asked emerged, yet the approaches that were used to address these questions diverged.

A number of talks focused on the overall dynamics of the cellular cytoskeleton. For example, Cécile Sykes discussed reconstituting the actomyosin cytoskeleton within liposomes, and Marileen Dogterom described her work reconstituting the microtubule cytoskeleton within microfluidic chambers. In these experiments, the addition of a relevant motor, either a myosin or a dynein, dynamically perturbs the system. Global aspects of organization are the readout, such as the centering of the microtubule aster within the space. More broadly, Fred MacKintosh, David Weitz and Christoph Schmidt discussed fluctuations of the overall cytoskeletal network within the cell, an ATP-dependent effect described variously as ‘active stirring’ or ‘active diffusion’. MacKintosh proposed that the cellular cytoskeleton is a network under internal tension due to molecular motors and crosslinking proteins poised at a critical point, meaning it is highly responsive and tunable. On the molecular level, Matthias Rief brought some insight to the problem by discussing how active forces influence the dynamics and strength of individual actin-filament-crosslinking proteins that organize such cellular actin networks.

Paralleling these talks – emphasizing network dynamics that model the cytoskeleton as a whole – were others that focused on intricate regulatory mechanisms leading to localized activation in order to yield compartmentalized function. Roop Mallik, Ewa Bielska and Erika Holzbaur discussed mechanisms that regulate molecular motor function on individual organelles to provide temporally or spatially specific localization. In a similar vein, Sam Reck-Peterson and Tom Surrey discussed mechanisms to localize motors specifically to the tips of microtubule polymers.

In keeping with the varied nature of the questions that were asked, there was also an exciting range of scientific approaches employed to answer these questions. Many talks discussed live cell imaging or single-molecule approaches, including TIRF microscopy and optical trapping. Meg Titus, Justin Molloy and Claudia Veigel discussed recently discovered myosins, including one from the parasite *Leishmania*. Motor-dependent remodeling of the cytoskeleton *in vivo* was addressed by Vladimir Gelfand, whereas Joe Howard discussed motor-dependent flagellar beating. Overall, there continues to be excitement in reconstituting and manipulating biological mechanisms *in vitro*, such as the work of Gijsje Koenderink and Margaret Gardel on actin and actomyosin network reconstitution in order to study the factors that govern the underlying network connectivity.

There is also a growing interest in using mathematical modeling as a rigorous test to determine how deeply we understand a given process. Alex Mogilner discussed computational modeling of mitotic spindle self-assembly, focusing on a force-balance model. But Iva Tolic brought up what she termed the ‘paradox of force balance’, referring to evidence suggesting that we do not yet know all the forces acting on a spindle.

From the first talk, Enrique De La Cruz – fighting jetlag to discuss the dynamics of actin filament severing – the organizers

<sup>1</sup>Department of Molecular Biophysics and Biochemistry, Yale University, 260 Whitney Avenue, New Haven, CT 06520-8114, USA. <sup>2</sup>Department of Physiology, University of Pennsylvania, 415 Curie Boulevard, Philadelphia, PA 19104-6085, USA.

\*Author for correspondence (enrique.delacruz@yale.edu)

emphasized that one of the goals of the meeting was to promote thoughtful discussion. The meeting's small size (34 participants) and the generous discussion periods that followed each talk fully facilitated this goal. Resulting conversations were lively and usually continued over tea breaks with scones and clotted cream, amazing meals and beers.

Finally, the site itself significantly contributed to the success of the meeting. Scientists – usually most comfortable in the lab – were treated to four days in a manor house in the South Downs of England, a conference facility closely resembling Downton Abbey, enhanced by a built-in on-site pub and an amazing art

collection (together with tours of the house and grounds). What more can you ask for?

Perhaps the best way to assess the success of this type of meeting is the number of ideas that are generated and the number of new collaborations that are sparked from interactions and discussions during the workshop. By these measures, the meeting appears on track for success. In summing up the meeting, Meg pointed out that the technology to tackle difficult problems is improving, allowing us to address complex physiology. However, biology continues to surprise us, leaving many questions yet to explore as we continue to navigate the cell.