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Editorial

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New Biological Frontiers Illuminated by Molecular Sensors and Actuators

From June 28–July 1, 2015, the Biophysical Society hosted a thematic meeting in Taipei, Taiwan entitled "New biological frontiers illuminated by molecular sensors and actuators." The meeting brought together a diverse group of biophysicists from all around the globe who specialized in various disciplines, including protein engineering, advanced fluorescence imaging, mechanobiology, neuroscience, materials science, and nanotechnology. Approximately 100 participants shared their discoveries and work, which revealed a recurring theme: the importance of looking to nature for inspiration and solutions. In this issue of *Biophysical Journal*, we present four perspective articles by participants of the Taipei meeting that summarize the current state of the field and its future prospects (1–4).

Molecular sensors came to prominence with the discovery of the green fluorescent protein (GFP) in jellyfish. Since those early days, researchers like the keynote speaker Atsushi Miyawaki (RIKEN, Saitama, Japan) have developed fluorescent proteins spanning the color palate from cyan to far red. Furthermore, they have enhanced these proteins to exhibit unique optical properties, such as photoactivation/switching and bioluminescence. The clever integration of fluorescent proteins into biological systems means that fluorescence can be equated to a biological state or function. A particularly visually attractive application from Miyawaki's work is the cell cycle indicator Fucci (5). Alternatively, fluorescent proteins can be transformed into sensors when the fluorescence is placed under the control of ligand binding. Miyawaki presented the example of UnaG, a protein found in eels that becomes fluorescent upon bilirubin binding (6). Perhaps the most famous fluorescent protein sensors are the calcium sensors, which gave rise to the discovery of calcium spikes and waves. Thus, it is fitting that, in this collection on sensors and actuators, Suzuki, Kanemaru, and Iino review genetically encoded calcium sensors to monitor spatiotemporal dynamics in intracellular organelles (3).

The development of sensors and their integration with advanced fluorescence techniques goes hand-in-hand. Noteworthy cases are Förster resonance energy transfer (FRET) and intravital imaging in live animals. Hirata and Kiyokawa first reviewed the design of single-chain FRET biosensors to monitor the activity of kinases, proteases, and GTPases and then explored the possibility to use these biosensors in transgenic mice (1). They then discussed in detail how intravital imaging technology can be optimized for FRET sensors. While there are still technical challenges to overcome, biophysical measurements with the aid of molecular sensors in living animals are the new frontier in cell biology, immunology, tumor biology, and neurobiology (7).

As the implementation of colorful sensors vividly reveals the spatiotemporally dynamic nature of cellular signaling, the obvious next step is to decode these complex observations by probing causal relationships between the spatiotemporal profiles of cellular signaling and biological outcomes. To achieve this, it is imperative to perturb a given signaling pattern at the right time during the signaling events and at the right place inside living cells. It is for this reason that the meeting focused on both sensors and actuators, an inseparable pair, to manipulate a molecular process and record the cellular response at the same time. To manipulate cell signaling at will, Yu-Chun Lin and Toru Komatsu introduced chemical dimerization tools, which exploit bacterial compounds to induce the controlled binding of two proteins. Meanwhile Michael Lin reported on optogenetics tools where engineered, light-sensitive proteins derived from a coral family undergo conformational changes upon photoillumination. Together with an introduction of such optogenetics molecules, Niu et al. describe biophysical prospects of these systems (4).

An emerging topic that was strongly represented at the conference was sensors and actuators for mechanobiology. Sensors for physical forces such as membrane voltage and cytoskeletal tension have been reported previously and we now have the first sensors that report intramolecular forces using a spider silk protein (8). Khalid Salaita presented novel optomechanical actuators that exert piconewton forces onto cells at nanoscale locations (9). The *Perspective* by Allen Liu looks at a range of technologies, including

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optical, magnetic, and acoustic control of cell signaling processes (2).

With these molecular tools in hand, an elegant example of combining sensors and actuators (10) was presented by Adam Cohen, who developed all-optical electrophysiology based on voltage-sensitive proteins from microbes (11). These are, however, just a subset of the many intriguing presentations at the meeting that fully justified the title "New biological frontiers illuminated by molecular sensors and actuators."

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