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## REPORT – Biophysical Society Meeting 2017: Eric Betzig "super resolves" the way to ground-breaking science

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The 61st Biophysical Society Annual Meeting took place in New Orleans, Louisiana, USA on February 11-15 2017, organized by the Biophysical Society.

The Biophysical Society – BPS annual meeting is a fantastic event. Scientists interested in Biophysics should attend this meeting at least once in their life time. This is especially true for students. Students may be already used to national or to some small-size international conferences in Biophysics. At the BPS meeting, first-time attendants may feel overwhelmed by the amount and quality of the science presented. Thousands of posters, dozens of commercial exhibitors, hundreds of oral presentations. It is quite common that your preferred sessions overlap in time, so be prepared for it!

The 61st Biophysical Society Annual Meeting took place in <u>New Orleans</u>, Louisiana last February. It covered many different topics, reflecting the multidisciplinary approach to science shared by biophysicists: protein structure and function, electrophysiology, muscle physiology, single-molecule

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methods, nanotechnology, membranes... It is impossible for a single person to select the highlights for even half of those topics. I would like to mention a few, although, of course, these are biased by my own personal interests.

I was impressed by the advances in the <u>manipulation of single proteins</u> using magnetic and optical tweezers techniques. For instance, the laboratory of Julio Fernández at Columbia presented results showing that single unfolded proteins slowly lose their ability to refold just by keeping them unfolded. The mechanisms behind this surprising behavior are currently under investigation, although it seems to involve oxidation of side chains in the protein. I also had the opportunity to attend a very interesting thematic session about <u>Piezo channels</u>. These enticing molecules support mechanosensation by detecting variations in membrane pressure, which lead to changes in the conductance of the Piezo pore. Results were presented that link mutations in Piezo channels with loss of <u>proprioception</u>, our ability to know where we are in relation to our environment. Proprioception is something that we take for granted, but it isn't obvious at all. Ardem Patapoutian from Scripps showed a shocking video of a patient who lacks proprioception and, as a result, is not able to stand. These new findings put us in the way to be able to treat these patients by targeting Piezo channels.

But the absolute highlight of the conference was the National Lecture, delivered by Eric Betzig. National Lectures at the BPS meeting are impressive events on their own. The National Lecture is given by a top scientist, in many instances a Nobel Prize awardee. The room is huge, probably hosting over 2,000 delegates. I appreciate that giving such a lecture brings in many challenges. It has to be general, while showing top-

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notch science. And yet, it is an evening session, where the speaker must engage an exhausted audience that has been discussing science since 8:30 am... Not easy!

I cannot stress enough how amazing and motivating Betzig's lecture was. He presented his milestone contributions to the field of <u>super resolution microscopy</u>. He was awarded the 2014 Nobel Prize in Chemistry for developing PALM microscopy. One may understand from Betzig's talk that this award was too preliminary because this technology is not well-suited for live-cell imaging in 3D. Indeed, he stressed that wide field and confocal microscopy techniques are limited because: i) they expose cells to a lot of photons (although most of them are not used to build the image) leading to photodamage of the cells, ii) they require transfection and labelling in non physiological conditions to introduce bright fluorophores in the cell, and iii) they require working with isolated or even fixed cells that have lost their homeostatic environment. Betzig described how he has been addressing all those limitations by developing different forms of <u>structured illumination</u> microscopy and <u>light sheet</u> microscopy. The movies shown by Betzig ware captivating. Cells in their native environment can be visualized in real time at resolutions below Abbe's diffraction limit in 4D. I had the impression that these developments would be enough to award Betzig a second Nobel Prize.

But on top of Betzig's contribution to light microscopy, his **unconventional career** is also exemplary.

Betzig would love to see academic life drifting away from bureaucracy and heavy teaching loads, to bring professors back to the lab. Indeed, he was never attracted by the traditional academic career. After getting his PhD in Physics from Cornell University, he joined AT&T Bell labs. It was during his time at Bell labs that he started thinking about ways of breaking Abbe's diffraction limit when imaging biological samples at room temperature. When Bell labs closed, he was first unemployed and spent some time as a house husband. Later, he worked for his father's company developing novel industry instrumentation with little commercial success. He quit and moved back to unconventional science. Using equipment discarded by Bell labs, installed in the living room of his friend and colleague Harald Hess, they both provided the first experimental evidence that PALM could be used to break the diffraction limit in light microscopy. They used their own savings to fund the project.

Soon afterwards, opportunity kicked in. The Howard Hughes Medical Institute (HHMI) launched his own research campus, Janelia Farms (nowadays Janelia Research Campus), in Virginia, US. The HHMI was interested in supporting unconventional scientists and providing them with funds to run a small research group, fully devoted to explore ground-breaking ideas -no grant writing, no teaching duties, no administrative service. Ten years later, Betzig's story of success shows that the HHMI's recipe works. During his lecture, Betzig was very thankful to the HHMI and very lively encouraged people like him to apply to Janelia... and proposed that the whole system should learn from this experience.

**55** ...the whole academic model of taking somebody from their postdoc, who finally is a really great researcher, and rip them out of the lab and make them basically the CEO of a small non-profit as an Assistant Professor... that seems f... stupid to me, I'm sorry!

Betzig said at the very end of his talk. It was late in the evening, but people cheered and applauded for a long time! I think we all wanted to be Betzig at that time. I for sure did.

Any student should watch Betzig's National Lecture, available *online*. Do not miss either Betzig's biographical note on the Nobel Prize website.

Hopefully I've provided enough reasons for you to attend the 62nd BPS meeting which will be held in San Francisco in February 2018. And maybe also to follow in on Betzig's footsteps!

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