

***Special Issue: IUPAB2024 Congress in Kyoto******Commentary and Perspective (Invited)*****Feeling a nanoworld with optical tweezers: Hands on training at IUPAB 2024**Zuzana Johanovská<sup>1,2</sup><sup>1</sup> J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences, 182 23, Czech Republic<sup>2</sup> Faculty of Mathematics and Physics, Charles University, 121 16, Czech Republic

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When I was asked to report on my training experience, I realized very early on that the hardest part will be figuring out how to grasp the subject. Not to mention, as a PhD student in the second year, I currently have next to zero experience with writing in an academic style. But even if I have some, I'm not sure how to handle a situation where I have to objectively describe subjective impressions and opinions. So I decided (as you can already see) to go in the direction of some kind of commentary. Please take it as such. At some points, I will try to cite and substantiate the information I present, but the rest is heavily influenced by the perspective of one single person at the beginning of a scientific career. I hope that for more experienced readers, it can still be an interesting insight into the world of today's beginners. But I can imagine you'll recognize some similarities with your own stories—just recall its previous chapters.

Let me open this comment by setting the scene. As an early explorer, it is easy to feel lost and uncertain in many ways. Is the topic I am studying really meaningful? Am I good enough to keep up with so many smart and dedicated people I see all around me? Is this career compatible with other parts of my life that I want to live? And will I get a chance to work in this field when I finish my Ph.D. or postdoc?

There are no answers to these thought experiments; we just have to wait and see what the future holds. Of course, it will be greatly influenced by our willingness to learn, persistence, and general openness, but it is not only that. There are factors that cannot be predicted and that can only be influenced to a limited extent. There are more than enough negative ones; that's why it's always nice and encouraging when we encounter some positive stimulus from the environment. Not only because it at least slightly increases our chances of succeeding in our academic journey, but it can also simply bring new motivation and encouragement. And it seems to be a pretty scarce commodity these days. Also I believe there is a proportionality between how much people can grow and the opportunities they are given. The same is said to happen to turtles: if you buy them a big aquarium and give them enough space, they will grow (I prefer not to try to find a citation for this statement because it would be a shame to ruin such a nice analogy with a possibly disappointing truth).

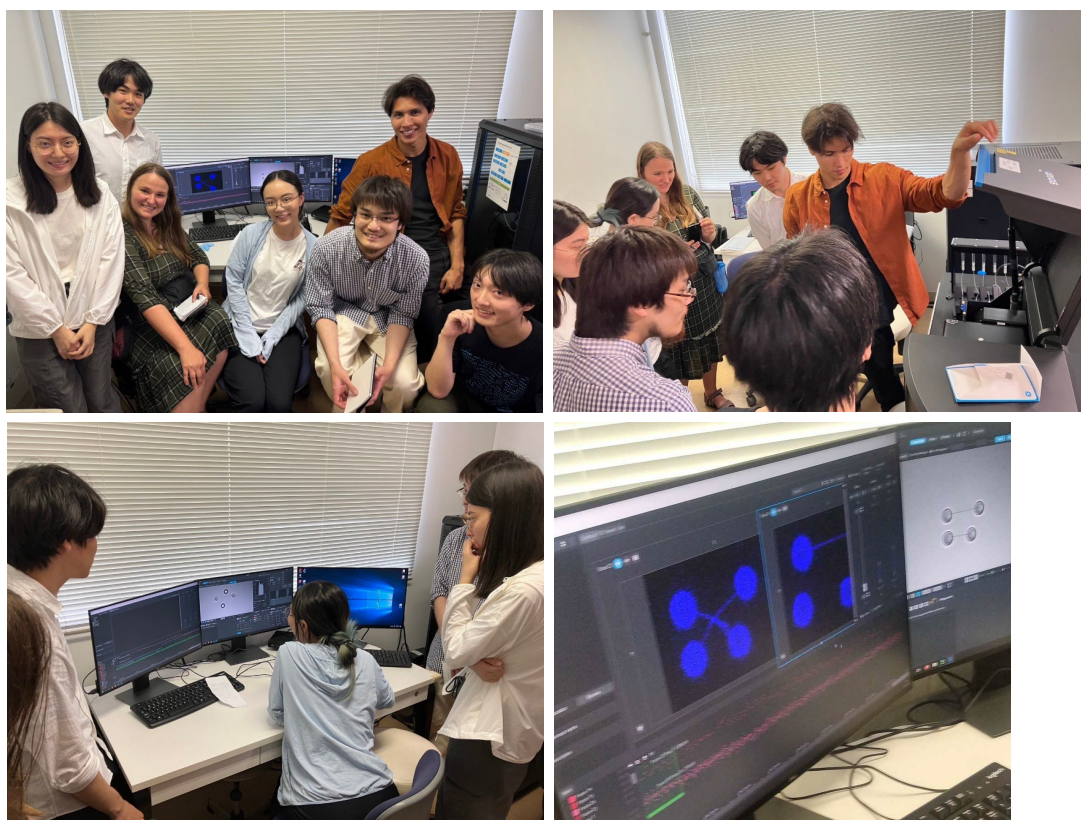
Being able to attend such a large conference as IUPAB is already quite a significant opportunity, and I feel very privileged that, thanks to the student grant from my university, I have been given the chance to be one of the lucky young people who were let to get there literally from the opposite end of the world. I really considered this chance as a gift, so when I found out that there was also another possibility to learn some new technique in the hands-on training program, I did not hesitate and gladly applied for it (and even more gladly accepted the invitation when I was one of the selected participants). And now, before I absorbed all the new experiences I brought back from Japan, I am already having another opportunity: to be the one to share the experience of this nice project. I am mentioning all of this to show that some opportunities are like snowballs. You start with something nice and small, and suddenly other chances are piling up. And at least in my case, the hands-on training associated with the conference seems to have a tendency to make these snowballs.

Corresponding author: Zuzana Johanovská, J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences, Dolejškova 3, 182 23 Prague, Czech Republic. ORCID iD: <https://orcid.org/0009-0007-4170-4214>, e-mail: [zuzana.johanovska@jh-inst.cas.cz](mailto:zuzana.johanovska@jh-inst.cas.cz)

To illustrate the possible impact of hands-on training, I will quickly introduce a program provided by LUMICKS, in which I participated in: Real-time single-molecule experiments with optical tweezers and correlated fluorescence microscopy. It was not the only possibility (in fact, the variety of topics was quite amazing in itself, from computational projects to experimental ones), but for me, it was most related to my research topic (dependence of mechanical properties on the structure of biological membranes). However, other participants' projects include nucleic acids, proteins, biomechanics, molecular motors, etc. Which shows at first glance how versatile this technique is.

While introducing the technique, our lecturer Loïc Chaubet from LUMICKS reminded us of the motto "seeing is believing, but feeling is the truth." It is a great analogy for optical tweezers because this instrument allows both direct manipulation of small objects and, at the same time, observation of the sample, which is completely non-invasive (as the name suggests, it is an infrared beam that optically acts on objects with a difference in refractive index from the surroundings) [1]. And not only you can control the position; since the optical tweezers act like a kind of spring, there is a possibility to directly measure the forces in the system in the order of piconewtons. The scale of these experiments is in micrometers, and with a few clever ideas, you can easily manipulate for example individual strands of proteins, nucleic acids, etc., which are even smaller [2–4]. This ability to "touch" the microworld opens up many possibilities, and the number of publications using this technique appears every year, sometimes even in a novel context [5]. But there are certainly still many projects that could benefit from these measurements, so spreading the word about such a possibility is definitely useful.

During the training, we all tried the basic operation of the machine for ourselves; we saw how it was all set up and even performed some illustrational experiments (Figure 1). I personally have already encountered this technique little bit before; however, the explanation from the expert, the consultation of specific parts of the machine, my project, etc. were definitely useful for me anyways. For others in the group, the positive effect was probably even greater, as most of them met this technique for the first time. But regardless of previous experience, each of us left with something new in mind (on my part, it was an alternative way to deal with some of the complications that arose in the system I'm interested in). Some of us also agreed to meet in a conference afterwards to learn about our projects (because from the discussion in the breaks, few of us realized that some of our projects had some parts in common), and we were all assured that we could contact our lecturer if we got a chance to work with the tool. So as a bonus, we got to experience some nice networking at its best.



**Figure 1** Illustrative images from Hands on training at Lumicks optical tweezer

And then came the conference. Just for the record, I counted the number of times I saw the use of optical tweezers in a presentation or poster. I got to number six or seven and you also have to take into account that I definitely covered only a small part of the whole event. So all the early-career researchers who had no prior experience with this technique had a much better idea after the hands-on training of what their more experienced colleagues were doing and why they chose to go that way in all these situations and all of us can from now on initiate meaningful discussion about the topics.

Conferences are about gaining new knowledge and expanding knowledge, and both were very nicely enriched by these hands-on experiences. It is very useful for the future profession to map out all the technological possibilities that can be used and not rely only on experiments carried out in home laboratories. After the hands-on training, each of us suddenly has a pretty concrete idea of a technique that was previously unknown to most of us but which can potentially be quite useful. Without this simple way to reveal it, there would probably be a hesitation as to whether something like this is worth the time, energy, and resources to try. But a simple, direct demonstration is better for that decision than thousands of words in articles. As such, experience makes it very easy to gain insight into the benefits and limitations of possible experiments. It may not be necessary for your current research topics, but maybe someday it will be. And we are now at least little bit ready for it. We will all remember, at least, the basics of what we saw. Seeing is believing, but feeling is true, and this is true not only for micromanipulations but also for learning. And scientists, especially young ones, should strive to explore the full range of research possibilities so that one day continue to develop new approaches and introduce new perspectives. It doesn't happen overnight, but it can happen slowly every day—with every small step, interesting experience, or kind word from someone who takes the time to help you learn something new. And the best part is that it doesn't end there.

That's why we travel and do science in the first place—to inspire ourselves and then pass on the inspiration to others. To return home and spread the new insights and ideas we have seen. And I am very grateful for the privilege of being an active part of this process now.

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## References

- [1] Hill, F. R., Monachino, E., van Oijen, A. M. The more the merrier: high-throughput single-molecule techniques. *Biochem. Soc. Trans.* 45, 759–769 (2017). <https://doi.org/10.1042/BST20160137>
- [2] Kurniawan, Vos, B. E., Biebricher, A., Wuite, G. J. L., Peterman, E. J. G., Koenderink, G. H. Fibrin networks support recurring mechanical loads by adapting their structure across multiple scales. *Biophys. J.* 111, 1026–1034 (2016). <https://doi.org/10.1016/j.bpj.2016.06.034>
- [3] Siahaan, V., Tan, R., Humhalova, T., Libusova, L., Lacey, S. E., Tan, T., et al. Microtubule lattice spacing governs cohesive envelope formation of tau family proteins. *Nat. Chem. Biol.* 18, 1224–1235 (2022). <https://doi.org/10.1038/s41589-022-01096-2>
- [4] Candelli, A., Holthausen, J. T., Depken, M., Brouwer, I., Franker, M. A. M., Marchetti, M., et al. Visualization and quantification of nascent RAD51 filament formation at single-monomer resolution. *Proc. Natl. Acad. Sci. U.S.A.* 111, 15090–15095 (2014). <https://doi.org/10.1073/pnas.1307824111>
- [5] Muir, K., Batters, C. H., Dendooven, T., Yang, J., Zhang, Z., Burt, A., et al. Structural mechanism of outer kinetochore Dam1-Ndc80 complex assembly on microtubules. *Science* 382, 1184–1190 (2023). <https://doi.org/10.1126/science.adj8736>