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Imaging, Manipulation, and Analysis of Biomolecules, Cells, and Tissues IX

Daniel L. Farkas

Dan V. Nicolau

Robert C. Leif

Editors

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Introduction

Believing in Seeing, *Vingt ans après*

As chairs for an exciting interdisciplinary conference featuring new advances in optical bioimaging, we feel blessed to just organize/introduce the talks and edit the resulting proceedings, while aiming for the highest quality in both. Thematically, we try to cast a wide net, resulting in the title Imaging, Manipulation and Analysis of Biomolecules, Cells and Tissues. The roman numeral IX following the title implies that this is our ninth year, but in fact it is our twentieth. This usually is a milestone, and calls for a look back, with an eye on distilling something useful for planning purposes, especially since “the best way to predict the future is to create it” (to underscore the differences between disciplines, this quote is attributed to Dennis Gabor, Alan Key, or Peter Drucker, depending on one's background and readings being in physics, computers or business, respectively).

We are fortunate to work in an area of science and technology that is evolving very fast, to the point that it even justifies a new name: biophotonics. Many exciting advances in the field came from other areas of technology that were developed by target-oriented, extremely well-funded people in space exploration, telecommunications, defense, and nanotechnologies, to name a few. Other exceptional tools, such as femtosecond lasers, enabled new (but brilliantly long-predicted) approaches including multiphoton excitation microscopy. We had the first talks on this in our conference, but very quickly, it grew into its own very successful conference. The same applies to other fast-developing areas such as optical coherence tomography and its applications, and fluorescent proteins and their family (which brought our field the ultimate scientific recognition, Nobel Prizes to Drs. R. Tsien, O. Shimomura and M. Chalfie).

Perhaps even more importantly, biophotonics is on the brink of changing some important clinical areas by the new approaches it brings to major unmet needs. This is an evolution in the right direction because twenty years ago engineering-oriented meetings, such as those organized by SPIE tended to accentuate the technical virtuosity, with usually the last slide stating something along the lines of “and this could be useful in cancer research”. Nowadays, presentations are not only more polished and continuing to advance the technologies, but they also focus much better on major challenges and the large set of requirements that need to be simultaneously met in order to achieve something meaningful. The application areas range from cancer (the perennial “grand challenge” on which progress has not been impressive) and cardiovascular disease, the biggest killers in our society, to areas that were not even in existence when we got started two decades ago: stem cells and cellular therapies, high throughput screening/sequencing, molecular diagnostics, and so on. Indeed, amazing results have been demonstrated in the lab (and reported in our conference through the

years): single molecules visualized in action (in a dish), whole genomes sequenced by optical means, cells moved around by laser beams into interesting action, entire (small) organisms imaged in 4D and sorted by features, single cancer cells captured in their first step towards setting up metastatic colonies (in small animals, in vivo), and many more. There is much cleverness deployed and promising many trends in these, and it is almost unfair to single out a few. Therefore, let us focus here on something of more general translational significance; how and when will all this yield something that will save lives and improve the human condition? More specifically, how do we go from impressive performance in the laboratory (femtosecond temporal and nanometer spatial resolution, molecular specificity) to equally impressive results in the clinic?

Complex disease will not yield to reductionist approaches, and molecular-specificity cellular-resolution imaging in the patient will be needed to effectively address such a challenge. This cannot (yet) be done, mostly because markers (such as quantum dots), big lasers, and other intense tools cannot be brought into the clinic except for ex vivo analyses. It is safe to predict, though, that if it can ever be done, optical imaging is likely to lead the way, as (a) light is a very powerful investigational tool and (b) all other medical imaging methods (x rays, MRI, ultrasound, etc.) seem severely limited in spatio-temporal performance and even specificity. It is vastly more difficult to image in a patient than in a dish, and not only for regulatory reasons; however, some of the necessary elements are already out there, being improved, fine-tuned, and sometimes unveiled at our conferences. For inspiration, let us think Mars Rover: we can image today dust on the Red Planet far better than we can image inside a human being who is in serious need in our best hospital. This does not feel right, and points the way towards where we should focus our efforts in the next twenty years. Luckily, there is a great supply of talented young scientists ready to do this, hopefully supported by enlightened governments, businesses, and unconventional sources. Let us hope that the results will be no less spectacular than those imagined by early science fiction, such as the influential sixties movie *Fantastic Voyage*, where a minified interdisciplinary group of scientists navigate in the body to the site of a life-threatening problem, and eliminate it with focused laser blasts. We have to keep believing in seeing: with lab-derived smart tools, at the right location (in the body), with performance far exceeding that of the human eye. This should allow finding problems early, guiding intervention, and achieving better outcomes, while also saving significantly on the cost of healthcare.

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