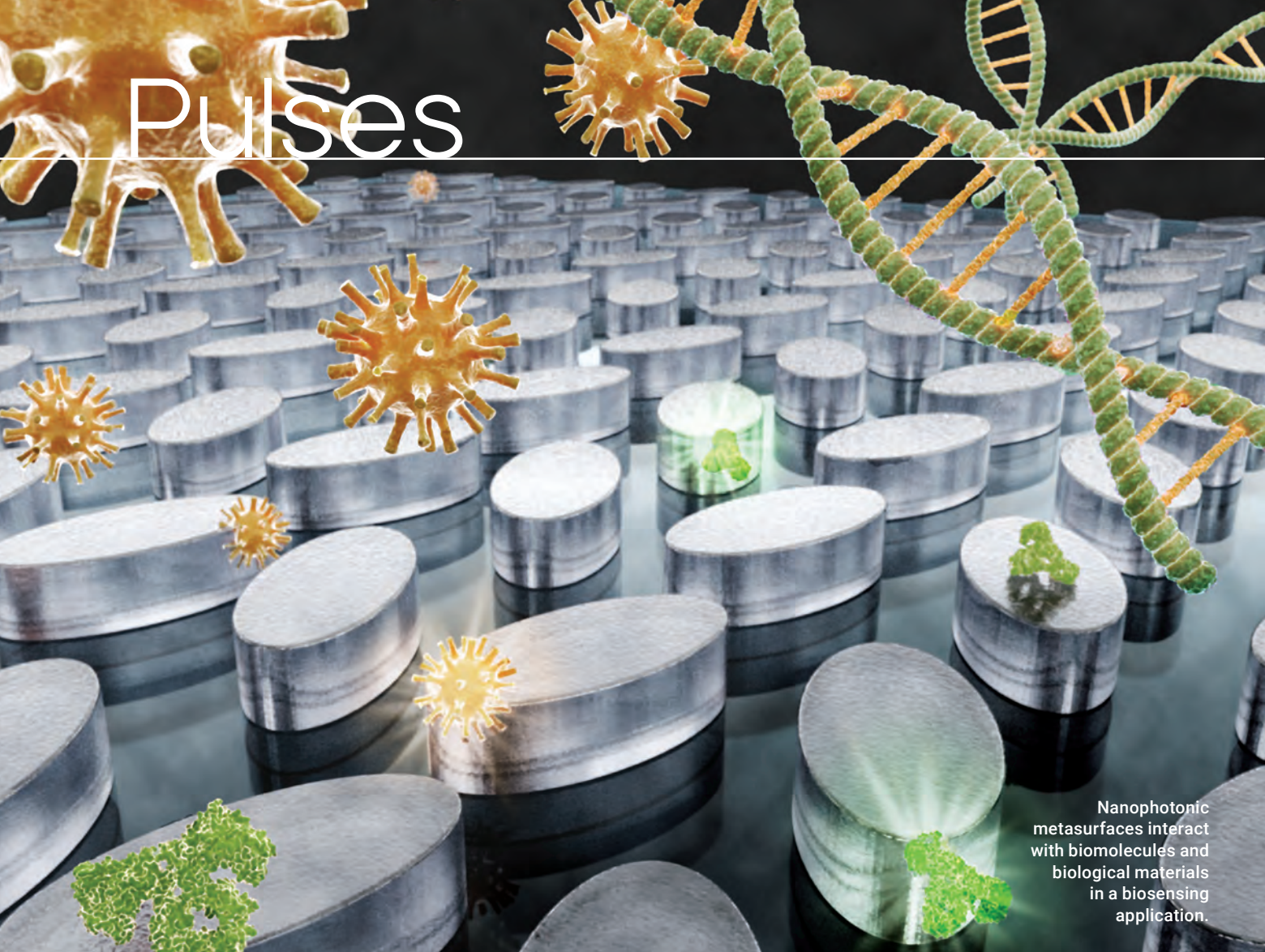


Pulses



Nanophotonic metasurfaces interact with biomolecules and biological materials in a biosensing application.

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CONVERSATIONS

Biosensing and Bioimaging with Nanophotonics

At the Optica Sensing Congress, **Hatice Altug** will discuss the latest developments in nanophotonics for applications in the life sciences and biomedicine.

The Optica Sensing Congress will be held from 15 to 19 July in Toulouse, France. At the congress, Hatice Altug, École Polytechnique Fédérale de Lausanne, Switzerland (EPFL), will give a plenary talk entitled, “Integrated Metasurfaces for Biosensing and Bioimaging.” She plans to cover her team’s latest research using nanophotonics and integrated metasurfaces to develop novel biosensing, spectroscopy and bioimaging systems. OPN spoke with Altug ahead of her talk to get a preview and learn more about the

potential for nanophotonic technologies to improve global health care.

Why is nanophotonics so useful for the life sciences and biomedicine?

Nanophotonics provides several fundamental and technological advantages compared with other approaches. I think the fundamental aspect is that nanophotonics enables us to confine light in nanoscale volumes and enhance the intensity of the confined near fields. Overall,

this increases light–matter interaction, which has been unlocking numerous different applications, in areas ranging from energy, to optical communications, to imaging and sensing, among others.

In our case, we utilize it for biosensing and life science applications, where the matter is biological substances. Biological substances—such as proteins, DNA, viruses, etc.—are typically very small in size; they are nanometric. By increasing light–matter interaction, we can have better performing bioanalytical devices. For instance, nanophotonics can enable us to achieve higher sensitivity, accuracy and precision for detection of low amounts of biomolecules from small volumes of samples.

A unique advantage of nanophotonics is that, as the optical components are shrinking in size and getting smaller, we can have easier miniaturization and integration and higher multiplexing capability. These features can eventually lead to high-throughput and portable systems that can go out more easily to the field.

Q. What are some of the most promising applications in sensing and imaging?

In my lab at EPFL, we utilize nanophotonics as one of the core pillars of our research, but we also combine it innovatively with complementary toolkits such as surface chemistry, data science, different imaging modalities, microfluidics and biopatterning. For example, we recently developed an optofluidic AI-aided mid-infrared biosensor to discriminate differently misfolded forms of disease proteins that are related to neurodegenerative diseases.

We also leverage newly emerging nanophotonic concepts to develop



Hatice Altug

A. Herzog

“Nanophotonics can ... achieve higher sensitivity, accuracy and precision for detection of low amounts of biomolecules.”

—Hatice Altug

powerful optical biosensing schemes. For example, one recently published work involves a novel metasurface concept that we call all-dielectric gradient metasurfaces, which provide high-Q resonances while also covering a very broad optical spectrum. In fact, having a high-Q resonance and broadband operation is difficult to achieve simultaneously. But, using this novel metasurface concept, we actually show that it can support both features on the same platform, and we used it for surface-enhanced infrared spectroscopy and strong coupling.

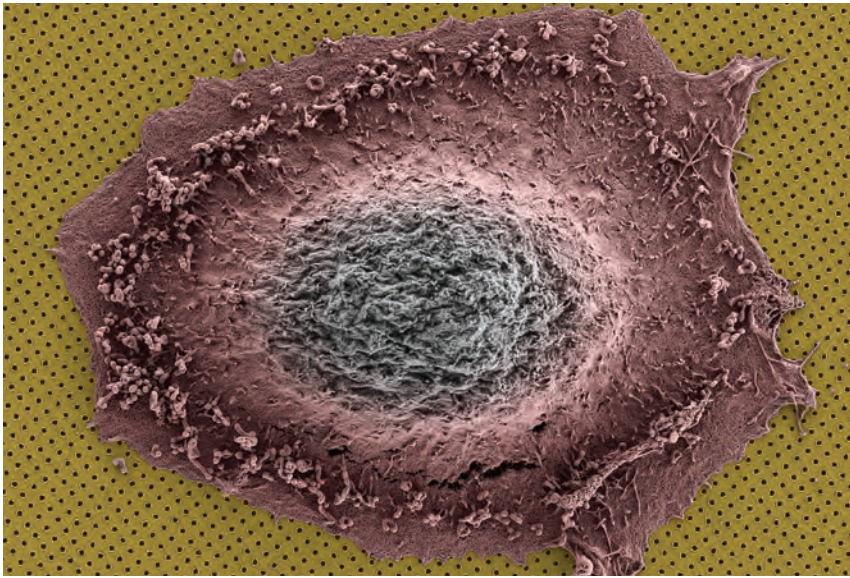
Q. Can you tell us about the advantages of integrating microfluidics in your work?

For biological applications, we typically need bioanalytical devices that can have automated and easy operation for the end user. Let's say, the user puts a drop of blood or urine sample into the sensor. The sample needs to be delivered to the active detection area, and this is where microfluidics can help us to handle the fluidic samples in a controlled and repeatable way.

Another advantage of integrating microfluidics is that doing so can lower the amount of the required sample, for example to just a few microliters. For diagnostics applications, this is important because we would like to have minimally invasive devices and collect samples as small as possible. In addition, microfluidics provide an aqueous environment, which is essential for biomolecules to maintain their proper biological functions, and also allow us to perform long-term monitoring on live cells by providing channels to deliver nutrition.

Q. What benefits have you seen from using artificial-intelligence and deep-learning techniques?

We have been using AI more and more recently in our work, as it provides multiple advantages. In our research we collect a lot of data, especially when we do spatially and temporally resolved imaging or spectroscopy. As a result, we have a large dataset and a lot of images to process, which can be cumbersome and slow to do manually. AI helps us to process these images and data more efficiently, accurately and reliably, in an automated way. For instance, in the case of our live cell



Colored electron microscope image of a single cell in an optofluidic nanoplasmonic biosensor incorporating gold nanohole arrays.

EPFL

projects, we train AI to recognize the boundaries of the cell to better analyze spatial-temporal secretion maps around the cells.

Another important advantage of AI is that once the network is trained, it can also make predictions. For example, in our recent mid-infrared work on misfolded proteins involving oligomers and fibrils, we trained the AI system using time-resolved infrared spectral signatures of the protein in different conformational states and in different mixture ratios. Then, when we give the AI the data of a new sample that it has not seen before, it can predict the composition of this mixed sample and identify how much of the protein is in oligomeric or fibrillar form.

Q What are the biggest challenges to developing the next generation of biosensing and bioimaging technology?

In sensing and imaging applications, we always strive to achieve high performance on multiple fronts, such as in sensitivity, resolution, throughput,

“ Since point-of-care systems can provide similar services at a lower cost and more rapidly, they can help to democratize health care and enable quick intervention. ”

—Hatice Altug

reliability, affordability, integration, etc. This is hard to accomplish, however, because whenever you achieve a good performance in one aspect, you typically sacrifice in another. Perhaps you have a very sensitive detection principle, but it might come at the cost of highly complex instrumentation or a bulky device. In this regard, nanophotonics can help to address this multi-parameter requirement space.

At the same time, with nanophotonics we need to consider the

cost issue—whether these nanophotonic structures can be fabricated in an affordable manner at a large scale. Another challenge is how to transfer a device out of the lab and ensure that it works reliably in the field and in the hands of untrained users.

Also, in biological applications, the samples are typically complex and the targets to detect are low in quantities—it’s like finding a needle in a haystack. So, the biosensor needs to have a very good selectivity and specificity.

Another challenge to success with new technologies is whether you can get them to be accepted by the end-user communities—perhaps this might be doctors or patients. Can your technology also pass through the regulatory steps, which are lengthy most of the time? And maybe the final challenge is getting a sustainable demand to maintain the need for your product.

Q Why are improvements to point-of-care diagnostics and personalized medicine so important?

One of the main driving forces for point-of-care diagnostics is to improve the accessibility of these technologies to a wide range of users and make diagnostics easier and faster in resource-limited settings, without the need for sophisticated laboratory infrastructure.

As we have seen in the case of COVID-19, you can have a point-of-care test and analyze your sample in the comfort of your own home. Since point-of-care systems can provide similar services at a lower cost and more rapidly, they can help to democratize health care and enable quick intervention for a better public health system at a global scale. **OPN**