Recovering from image distortion

Being able to visualize the functionalized surface of a nanoparticle with molecular resolution would be helpful for many fields. With the recently granted Innovative Training Network SuperCol, Peter Zijlstra is taking on the challenge to generate novel imaging tools.

It seems straightforward. You have a collection of identical nanoparticles and, to give them an additional property, you attach chemical groups to their surface. And as the particles are identical, their functionalized counterparts will be as well. Unfortunately, reality paints a completely different picture, says Peter Zijlstra, assistant professor of Molecular Plasmonics at the departments of Applied Physics and Biomedical Engineering. “Right now, we can only determine an average. We take a solution of the functionalized particles, we measure the effect and then we can deduce..."
the average number of functional groups per particle. But we know that in reality there are huge differences between functionalized particles. Both the number of groups and their distribution on the surface show a large variation."

For biomedical applications, such as sensing or drug delivery, it is crucial to have a well-defined, homogenous population of functionalized particles. Zijlstra: “We use functionalized nanoparticles for sensing applications that detect biomolecules, such as antibodies or inflammation markers, and we have noticed that each particle responds differently. Some particles hardly bind to the biomolecule, whereas others generate a very high signal and yet others perform somewhere in between. That is a real problem for these types of applications, but it is very hard to optimize the functionalization process when you have only average values to work from. We don’t know what we need to do to create a more homogenous distribution, because we don’t know what the actual distribution is. So it is clear that we need to know exactly what the particles really look like.”

SUPERRESOLUTION MICROSCOPY
That is why Zijlstra, who has a background in microscopy, is on the trail of superresolution microscopy. “A very powerful technique, but not yet for the study of our nanoparticles. As each particle acts like a fishbowl, the light gets scattered in all directions and the result is a distorted image.” That may sound discouraging, but not to Zijlstra. “We know that there is a particle that distorts the image, but because we know the shape and size of the particle we also know the nature of the distortion. So we should be able to work our way back and correct the optical image to show us what the particle really looks like. And when we know that, we can work towards the rational design of functionalized nanoparticles.

Then we can develop better optimization protocols and create opportunities for generating new functionalities that enable responsive materials or materials with superselectivity.” That is, in a nutshell, the program of the recently granted Innovative Training Network (ITN) SuperCol, which will be managed by Zijlstra and was initiated together with Ilja Voets.

Next to managing the consortium, Zijlstra will busy himself with cracking the relationship between the distortion of the microscopy image and the real distribution of the functional groups on the particles. He will also work on applying these concepts to switchable sensors. “The novelty of our approach is that we will combine measurements and models. We will compare experimental images of very well-defined particles with the models, and use that to correct the superresolution images. It all revolves around the shape of the ‘spot’. This is not perfectly round, because the particles distort the light and that is where we can extract information about the exact location of the functional groups. One of our aims is to develop software that can perform this interpretation step.”

"THIS IS ABOUT CURIOSITY-DRIVEN RESEARCH IN SUPER RESOLUTION MICROSCOPY AND COLLOID CHEMISTRY."

PERFECT FIT
The SuperCol consortium encompasses 8 academic partners and 11 companies and will use its approximately €4 million budget to train 15 PhD students over the coming four years. Why the choice for an ITN as a funding instrument? “This is about curiosity-driven research in superresolution microscopy and colloid chemistry, that will generate opportunities for applications in biomedicine and new materials. Moreover, through our contacts with companies, we learned that they urgently need people who are qualified in this area. It just all fits together perfectly and really matches the criteria for an ITN. And because this is such a broad challenge that requires various areas of expertise, you need critical mass to really have an impact and get things going.” Each PhD student will perform part of the research at one of the participating companies. “It is striking that most companies in the consortium do not work on biomedical applications, but are very interested in our research for other applications, mostly in materials. That shows the relevance of this ITN.”