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Nicoletta Liguori: "The ERC Starting Grant is an amazing opportunity to tackle the most ambitious questions at the fundamental level"

Nicoletta Liguori, Group Leader at ICFO since the end of 2022, has now received an ERC Starting Grant, one of the most prestigious European grants for early-career researchers. Over the next five years, this funding will allow her and her team to explore fundamental questions at the frontier of biophysics. Her project, called MARIONETTE, aims to understand how changes in the structure and environment of photosynthetic proteins allow them to regulate light-harvesting in plants.

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How do plants safely carry out photosynthesis and prevent photodamage when sunlight suddenly becomes too intense? This fundamental question remains challenging to answer, but Nicoletta Liguori is determined to implement new tools to do so. After completing her PhD at VU Amsterdam (Netherlands) and establishing an independent research line at the university's LaserLab supported by a competitive national grant, Nicoletta brought her expertise in ultrafast spectroscopy and molecular dynamics applied to photosynthesis to ICFO, where she now leads her own group as a Principal Investigator. Since the end of 2022, her team has been steadily pushing the frontiers of these methods to better understand how photosensory proteins work and, especially, how photosynthetic organisms regulate light-harvesting.

Nicoletta has now been awarded a European Research Council (ERC) Starting Grant -one of Europe's most competitive and respected funding opportunities for exceptional early-career researchers. The grant supports a five-year project in fundamental science, giving awardees the freedom to pursue high-risk, high-reward research of their choice. This marks a major turning point for Nicoletta and her group, who are hoping to now capture the molecular switches taking place inside the leaf in real time.

In this interview, Nicoletta walks us through the path she took in fundamental biophysics and how she ultimately achieved this grant.

The ERC Starting Grant marks the beginning of MARIONETTE. Can you summarize the idea of the project?

With **MARIONETTE**, we will implement and integrate in photosynthesis new approaches in advanced spectroscopy and molecular dynamics simulations that will allow us to change structure and environment at a molecular scale, and probe their effect on the function of photosynthetic proteins with an unprecedented level of detail, both in time resolution and at a structural level. This will allow us to understand how it is possible that, by tuning the microenvironment and changing the protein conformation of single photosynthetic proteins, plants are able to perform photosynthesis safely under the sun without photodamage.

What are the unknowns in the photosynthetic process that led you to choose this specific topic?

After many years of work by several groups, nowadays we finally understand what the key players are in how plants can activate and deactivate photoprotection. We know many of the proteins and cofactors involved. We know what changes in the microenvironment of the photosynthetic membrane are responsible for activating and deactivating photoprotection. However, all these processes occur at the molecular level, at the level of single proteins, and they involve changes in the excited-state dynamics of the pigments, which are characterized by ultrafast timescales. This means that there is a vast hierarchy of timescales involved, actually.

This hierarchy, coupled with the ultrafast resolution required to study the energetics of photosynthetic proteins and the (sub)nanometer resolution required to study protein conformational changes, altogether represent a highly challenging task to solve if we want to understand how photoprotection is activated in plants. That's why there are still many unknowns, like what are the molecular mechanisms that trigger photoprotection, what are the proteins domains involved, or what happens in the surrounding of photosynthetic proteins after sunlight intensity changes.

So, we need techniques to follow in real time these molecular, environmental and structural changes with the fastest resolution possible, as well as tools capable of simulating them. This is what we want to take into the field: a combination of novel approaches that will be able to study such small and ultrafast details across a vast hierarchy of timescales, to ultimately reconstruct the photoprotection activation in real time and step by step. More universally, we want to understand how the function of photosensory proteins are tuned in nature by changes of environment and structure.

You have been leading a group at ICFO called ï¿½Photon Harvesting in Plants a d Biomoleculesï¿½ for two years and a half. From that title, I would say that MARIONETT is really aligned with the research you develop in there. Is that really the case, and in hat sense?

Absolutely. Studying how photosynthetic organisms can regulate light harvesting and, even more generally, the topic of how photosensory proteins activate and regulate their function in different biological processes at the molecular level is the focus of our group.
What **MARIONETTE** and the ERC are going to allow us to do is to develop and implement novel tools to study that. MARIONETTE will be a combination of three different approaches that will be all new in photosynthesis. For example, it is going to be the first time that someone applies single molecule optical tweezers with force and fluorescence correlated data to photosynthetic proteins. We will also apply an innovative tool developed by our group to trigger rapid changes in the microenvironment of photosynthetic proteins and reconstruct their photoprotective response step-by-step. Finally, we aim to obtain a structural view of such processes combining an ad-hoc ?cocktail' of state-of-the-art molecular dynamics simulations methods. **MARIONETTE** will therefore allow us to study the correlation between changes of structure and environment and modifications in the energetics of photosynthetic proteins.
MARIONETTE will deliver the possibility to apply all these new set of techniques to the general goal of the group, that is, to study how changes of light, structure and the environment regulate the function of photosensory proteins.

You obtained an ERC Starting Grant on your very first application. What does this achievement mean to you and to your group?
First, I'd like to stress that this ERC really comes not only from my idea, but also from the effort of the whole group. In the last two years, we have worked really hard to obtain all the proofs of principle for the project. Super importantly, I'd like to thank deeply for all their incredibly kind, helpful and invaluable advices and feedback, all the outstanding researchers inside and outside my field who helped me and all ICFO departments, with a heartfelt thanks to ICFO Competitive Funding.
The ERC starting grant is an amazing reward for the whole group because now we will have the chance to focus on advancing fundamental science for five years in a more relaxed way. I am very grateful to the ERC for this because, for us, this means stability and access to great resources to perform fundamental science. I really believe **this is an amazing opportunity that Europe gives to young teams and junior researchers like us to tackle the most ambitious questions at the fundamental level**, which is extremely necessary to keep advancing science. I just hope more similar chances to focus in a relaxed and passionate way on fundamental science were given to the research community.

In the context of climate and energetic crisis, light harvesting is one of the molecular processes often explored in different fields. Do you think your project could have practical applications?
The most direct impact of MARIONETTE will be in fundamental science. As I have said, it is a

project designed to understand how environmental and structural changes at a molecular level can regulate in real time the switch between antenna and photoprotective functions in photosynthetic proteins. The main direct impact will thus be fundamental, to advance our understanding on how light harvesting is regulated in natural systems.
But, **on a very long term, this might also have an impact on** more applicative science. For example, there are many research groups that are designing novel **bioinspired systems for solar harvesting**. Perhaps some of the principles that we will investigate could be applied to improve the photoprotective properties of such devices. Or, maybe, studying and understanding what are the intermediate steps, the bottlenecks and interaction sites involved in the activation of photoprotection in plants could allow us to re-engineer light harvesting regulation from the very first steps and at the molecular level. In turn, this could increase the efficiency in the plants' utilization of solar energy.

I'd like to end with a more personal question: when did you know that you wanted to study science, and why did you choose this specific field?
I always liked science. When I was a kid, I spent hours watching documentaries and reading general scientific journals for kids such as Focus. Still, at that time I was in between liking architecture, fashion design and comics drawing, or science. But when I was 14 years old or so, I remember being in Napoli with my cousin and going to a bookshop with him. In there, I found the book of Stephen Hawking "The universe in a nutshell". I remember it was an aesthetically beautiful book to read, and all the topics inside were very catchy. I loved it, even if I could not understand many of the things it said.
At that point, I realized that I liked physics. And when I started the degree in physics, I realized that what I liked the most was biophysics. During my PhD, I was extremely fascinated about the possibility to understand how proteins, structural changes or changes in the interactions between a protein and its environment can explain many macroscopic processes that are so relevant for life. **The more I was in the field of photosynthesis, the more I was inspired by understanding how such small details are so relevant** for allowing photosynthesis to be performed so efficiently while preventing photo damage and, in the end, **for life on earth**. Now I hope that, with **MARIONETTE**, we will be able to study new aspects of how photosynthesis is regulated.

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Portrait of Nicoletta Liguori in her lab.