

Biomaterials and Biophysics

A conversation with Elisabeth Engel

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If anything in this multidisciplinary scientific world, I consider myself a *biophysicist by training*. I hold a M.Sc in Biochemistry and a Ph.D from the Biophysics Unit at the UPV/EHU. During one of my earliest scientific discussions with Prof. Félix M. Goñi, one of the founders of the [Spanish Biophysical Society](#), he replied to my news reporting that I could see the binding of the toxin we were working on to its receptor in cells: “very good, but we are biophysicists, we give numbers”. A few days after, I got those numbers, and there they are in my first scientific publication ([Cortajarena, Goñi, and Ostolaza, JBC 2001](#)), the binding constant and the number of receptors per cell, which amounts *exactly* to 3584 ± 284 ! This quantitative approach has been always present in my

scientific career. Then, I worked for 9 years at the Molecular Biophysics and Biochemistry Department at Yale University and 5 more at IMDEA-Nanociencia, in a very multidisciplinary environment with a strong physics component.

I developed my career progressively from fundamental protein mechanism-of-action studies, protein folding and protein design, to the application of protein engineering to the generation of protein-based functional nanostructures and biomaterials. My research has always been fed by different fields but I have been mostly fascinated by the natural world and by how complex machines and materials with amazing properties are made using biomolecules, composed of very simple building blocks and orchestrated by fundamental biophysical laws. My research interest is how to mimic Nature in the lab to build complex biomaterials, using simple bottom-up approaches and biophysical concepts. This is one of the main focuses of my current research group at the Centre for Cooperative Research in Biomaterials – [CIC biomaGUNE](#).

When I was proposed to tackle this topic of *Biomaterials and Biophysics* my first thought was that I needed to approach a scientist who complements my vision and fundamental perspective on biomaterials design; a researcher that could provide a more applied perspective of the field. This would allow a discussion of current challenges and unmet needs regarding the use of biomaterials, enhancing my biophysical perspective, and the consideration of real-life applications of rational bottom-up approaches for smart functional biomaterials design.

In this context I thought of Dr. Elisabeth Engel. She got her PhD in Medicine in 2003 in bone metabolism diseases. She worked as postdoctoral fellow at the Polytechnic University of Catalonia in Biomaterials for bone tissue regeneration, and is now full professor at the Materials Science department of this university. From 2012 she leads the [Biomaterials for Regenerative Therapies](#) group at the Institute for Bioengineering of Catalonia – [IBEC](#). Her research interests include the preparation and design of materials and scaffolds for *in vitro* and *in vivo* fundamental studies, and the provision of useful tools to assess mechanisms that govern cell behavior in regenerative medicine. Her group



DR. ELISABETH ENGEL.

conducts several transference and translational projects with pharma and biomedical device industry partners and participates actively in European projects.

During my conversation with ELISABETH I had the opportunity to discuss some questions that intrigue me in order to get a more integrated view of the field, aiming at building bridges between materials science and biophysics. We started talking about the current approaches towards biomaterials applications. Here ELISABETH agreed that they are mostly *trial-and-error* phenomenological approaches. However, she focuses on novel approximations that include systematic studies of the effect of biomaterials on tissues and pathologies, including tissue and cell line specificities, the acquisition of fundamental understanding and back to biomaterial redesign. This is an approach that she, among others, has pioneered and that she identifies as key for the future success of the field, since, as she affirms, “there are no inert biomaterials”. Here we agreed that the quantitative, physical, and non-phenomenological approach to biology, that biophysics takes, may have relevant contributions in the near future.

In vivo systems are very complex, multiparametric and dynamic, and we need to understand this complexity

And what about Nature? We reflected then on natural biomaterials. What do we need to learn from Nature? To this, she stressed that “in vivo systems are very complex, multiparametric and dynamic, and we need to understand this complexity”. We talked about how much of this complexity we are currently able to understand and parametrize in order to apply it for the design of biomaterials. “We know a lot from biomaterials, we know more and more about biology, and we need to integrate these two worlds, and I

believe that biophysics is a discipline able to integrate them. For this, we need more interdisciplinary teams”.

From the more fundamental perspective, there are many efforts invested in the design of novel biomaterials, but, what do we need to consider in order to get closer to successful in vivo applications? ELISABETH thinks that the most efficient way is to consider the application, talk to target users (clinicians) and carry out a joint development from the very beginning. Integration and interdisciplinarity seem to be again key aspects to help us to advance.

Looking to the other side of the coin, we discussed on how biomaterials engineering can be enriched by fundamental biophysical studies.

“Biophysics has the opportunity to generate new methodologies to help us to obtain and decipher experimental parameters related to biomaterials performance, that are currently limited at the biological level. This can be very relevant”. I asked ELISABETH about dynamics, considering that this is an

important characteristic of biological systems. “Yes, I believe that dynamics is very relevant, but complex. Currently we are not able to understand or design dynamic biomaterials that can mimic the dynamics of living systems”. This thought took us again to the key role of collaborative research: “New techniques that can be provided by other fields can give us important information about dynamics”. On the other hand, ELISABETH hopes that Artificial Intelligence and Machine Learning approaches will start to be applied in this field. “I believe that this will be an important turning point that will allow us to correlate all the knowledge that we have from different fields to start mimicking more real complex systems”.

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Here is where biophysics can also help to extract quantitative parameters from the current biological experiments

Finally, we embarked on the exercise of trying to unravel the future. The wish list is clear: We need biomaterials that are *complete*; i.e., that can perform *in vivo* as needed for their application and that all the required properties could be encoded and tuned based on a fundamental understanding of the biomaterial and its interaction with relevant biological systems. However, the reality tells us that “we are still far, very far indeed, and we currently do not have any biomaterial that fulfills all those

requirements”. The focus is now in using biomaterials that can signal the biological environment. “For that, we need to understand the physiology of the tissue at each condition and how the tissue evolves.” Here is where biophysics can also help to extract quantitative parameters from the current biological experiments. “Then, we can rationally design biomaterials that can control and/or modify the tissue environment to promote, for example, healing and regeneration”.

After our conversation, the conclusion is clear; the essence that keeps science moving forward:

“ There is still a long way to go in the field of biomaterials design, and researchers from different fields, we all have to walk together this path.

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