

## Appel à manifestation d'intérêt - Chaire Inserm

**Établissement/organisme porteur :** Inserm

Nom du chef d'établissement/d'organisme : Gilles Bloch

Site concerné : U1054

Région académique : Occitanie Est

**Établissements/organismes partenaires envisagés :** Université de Montpellier

**Nom du projet :** Computational protein design

**Mots-clés :** Synthetic biology, protein design, bioengineering, nanomachine

**Durée visée:** 4 years

**Scientific domain:** Synthetic Biology, Bioengineering, Structural Biology

**Section (s) CNU/CoNRS/CSS correspondante (s) :** CSS1 INSERM

### Strategy of the host institution:

As mentioned in INSERM's 2020 strategic plan, tomorrow's scientific challenges require multidisciplinary approaches such as those employed by synthetic biology (SynBio) to explore the different scales of organization of living systems, from molecules to organisms. SynBio seeks to engineer new biological parts, devices, and systems, or to redesign systems that are already found in nature. SynBio is revolutionizing our understanding of biology and will provide new disruptive tools for diagnosis and therapeutics, including personalized medicine. In that context, computational protein design can provide tailor-made proteins and protein complexes that can be used as diagnostics tools, new drugs, or assembled into dynamic systems to finely control cellular behavior.

### Strategy of the host laboratory:

The CBS (Center for Structural Biology) is an interdisciplinary INSERM-University of Montpellier-CNRS joint research institute conducting cutting-edge research in structural biology, biophysics and bioengineering in order to understand and exploit the physico-chemical mechanisms underlying biological processes, from the molecular and supramolecular levels to the cellular and organismal ones.

The CBS includes 13 research teams and several world-class structural biology and biophysics equipment including cryo-electron microscopy, NMR, crystallization, atomic force microscopy, nanomanipulation, advanced fluorescence microscopies, and bioinformatics facilities.

The CBS host several synthetic biology groups interested in bacterial engineering, cell-free systems, virology, protein engineering, DNA origami and DNA nanomachines. The institute now aims at expanding its synthetic biology expertise by recruiting a new research group with emphasis on computational protein design and protein nanomachines.

### Summary of the scientific project:

Computational protein design is revolutionizing the fields of synthetic biology and biotechnologies by enabling the design of artificial, protein-based systems with novel, tailor-made functions. Examples include in silico design of protein or small molecules binders, enzymes, artificial signaling

pathways, synthetic motor proteins and nanomachines. Applications include medical diagnostics, bioproduction, bio and cellular therapeutics, and more generally the engineering of bio-molecular systems performing sophisticated tasks at the nanoscale. Powered by recent advances in artificial intelligence, computational protein design has reached maturity, with the above-mentioned transformative applications now being within reach.

The recruited researcher will develop a project exploiting the recent breakthroughs in de novo, computational protein design, in synergy with the broad CBS interests. Research themes of interest include: (i) de novo design of genetically-encoded nanomachine, (ii) de novo design of protein-based sensing and signaling circuits operating in vitro or in vivo, with applications to diagnostics and therapeutics, and (iii) the development of new computational, deep-learning based approaches for the design of higher order protein assemblies and protein nanomachines.

The recruited researcher will have access to state of the art experimental (cryo-EM, super resolution microscopies, biochemistry and cell biology equipment) and computational facilities in the CBS and in Montpellier.

### **Summary of the teaching project : 15 lignes maximum**

The University of Montpellier supports the implementation of a scientific project in the field of computational protein design at the CBS by awarding a "starting grant" (junior chair) from its I-Site MUSE. The University of Montpellier (UM) offers as part of its Biology-Health Masters, an interdisciplinary "Quantitative Biology" (QBio) course taught in English offering extensive hands-on training on structural biology, biophysics, systems and synthetic biology. In that context, computational protein design is a key topic from which students training would benefit.

The teaching project of the INSERM chair (28h/y) will have to provide an overview of this fast-evolving field of research by: 1/ providing students an overview of the history and evolution of the field and its current theoretical approaches. 2/ Train students on the use of state-of-the-art computation tools for de novo protein design. This hands-on part will be possibly integrated to the Masters' practical courses, enabling a complete design/build/test cycle of the students' productions. These teachings will find their place not only within the Master's "Quantitative biology" of the UM but also possibly in UM masters targeted at bioinformatics.

### **Funding :**

ANR package	200k€
Co-funding*(Univ Montpellier)	100k€
Total project	300k€

\*source et montant

### **Scientific communication and dissemination:**

The project is expected to give rise to several publications in internationally, high-quality peer-reviewed journals, coupled with communication with the general public. The new computational tools developed during the project's course will be released as open-source software, available on GitHub and when possible, via a webserver interface hosted with the CBS support. We also expect the recruited researcher to seek active collaboration with other institute members and the larger scientific community in Montpellier, France and abroad that will result in joined publications. The researcher is also expected to pursue intellectual property protection for specific inventions if a commercial application is envisioned. Results of the work are expected to be presented regularly at international conference.

### **Open Science:**

We strongly encourage the researcher to publish in open-access journals. Publications will all be deposited in the HAL database. We will also encourage the use of preprints (e.g. BioRxiv). Software tools generated will be open-source and deposited in GitHub. All tools and methods will be shared with the local, national and international scientific community. DNA constructs will be made available through Addgene for distribution.

**Science and society:**

We encourage the recruited researcher to communicate with the general public through conferences and the annual “fete de la science” festival. The publication of a review article on computational protein design and its applications for more general audience (e.g. *Medicine et Sciences*) will be supported.

**Indicators:**

Teaching: active involvement and achievements of students, feedback

Research: number of publications, grants, number of recruited people

Knowledge transfer: patent, contract with private companies and creation of startup if applicable