PhD position · Université Grenoble Alpes · CEA Grenoble · Starting October 2026

Integrative AI models for *therapeutic peptide design*

Combining experimental fitness landscapes with generative structural design.

Host lab: BGE — Biosciences & Bioengineering for Health **Doctoral school:** ED ISCE - UGA

Scientific context and societal impact

Therapeutic peptides are an emerging class of biologics, with nearly one hundred approved drugs, capable of modulating protein–protein interactions that conventional small molecules cannot reach. This project develops AI-driven computational methods to design peptides against two targets of major public health relevance. **Influenza** is estimated by the WHO to cause 290,000 to 650,000 respiratory deaths globally each year and **Antimicrobial resistance (AMR)** was associated with an estimated 4.95 million deaths worldwide in 2019 (1.27 million directly attributable), and is designated by the WHO among the top ten global public health threats. In both cases, peptides offer a promising but under-exploited therapeutic modality, and the bottleneck is no longer synthesis or screening but the *design* of candidates that simultaneously satisfy affinity, selectivity and safety constraints. The methods developed in this PhD aim to address this bottleneck and, beyond the two case studies, to produce a general framework transferable to other peptide and protein design problems.

Approach

Two families of computational methods address therapeutic peptide design with complementary strengths and limitations. **Generative structural design**, AlphaFold-based hallucination, and sequence–structure co-diffusion models, exploits the geometric and chemical complementarity of a target binding site to generate structurally compatible sequences; however, because these models are trained on the Protein Data Bank, they are blind to the system-specific functional constraints and complex phenotypes (such as toxicity or membrane selectivity) that determine therapeutic viability. **Experimental fitness models** trained on high-throughput screening data (phage display, deep mutational scanning) directly capture sequence–function relationships as observed in the lab, but remain confined to the sequence space sampled during the experiment and lack structural guidance for extrapolation. The central methodological contribution of the project is to **couple these two families of models**: the experimentally learned fitness function is used as a differentiable constraint (classifier guidance) that steers the generative trajectory of the structural model, producing peptide candidates that satisfy both structural complementarity with the target and functional criteria derived from experiment.

Applications

Application 1

Anti-influenza peptides targeting the PA–PB1 polymerase interface

In-house phage display and structural design campaigns at CEA-IRIG will serve to validate the fitness–structure integration. Candidates will be evaluated by biophysical assays (BLI, TSA) at IBS, cellular viral-inhibition assays at Institut Pasteur, and X-ray crystallography for the best hits.

Application 2

Antimicrobial peptides — activity versus host toxicity

Public deep mutational scanning datasets on Protegrin-1 and Oncocin provide a benchmark for the multi-modal fitness model and for multi-objective generation along the activity/hemolysis Pareto front.

Research environment

The PhD will be carried out at the **BGE laboratory** (Biosciences & Bioengineering for Health, UGA / CEA / Inserm) on the CEA Grenoble campus, under the supervision of **Christophe Battail** (DR CEA) and **Guido Uguzzoni** (CR CEA). The project is embedded in an active interdisciplinary network: close collaboration with **Darren Hart** (DR CNRS, IBS/CEA-IRIG) for experimental phage display data and for biophysical and structural validation; with **Institut Pasteur** for cellular viral assays. The doctoral candidate will be encouraged to undertake research visits at partner institutions and to present at international conferences (ISMB/ECCB, MLSB, Biophysical Society).

Candidate profile

We seek a candidate with a strong background in **mathematical modelling and programming**. A Master's degree (M2R) in physics, mathematics, computer science or computational biology is required. Essential skills include foundations in *statistical physics* and *machine learning*, advanced programming in Python or Julia with experience in ML frameworks (PyTorch, JAX or equivalent), knowledge of probability theory, and familiarity with biological sequence analysis. Prior exposure to structural biology, generative models or protein language models is an asset but not required. Strong analytical skills, autonomy and interest in interdisciplinary research are expected. English proficiency at B2 level or above; French is not required.

Position & application

DURATION	3 years, starting **1 October 2026**
FUNDING	Doctoral fellowship of the **ED ISCE** doctoral school (MESRI — UGA). The position is conditional on selection by the doctoral school's competitive call.
SUPERVISION	C. Battail (DR CEA) — director; G. Uguzzoni (CR CEA) — co-supervisor
HOW TO APPLY	Through the **ADUM** platform; candidates are strongly encouraged to contact the supervisors in advance with a CV, transcripts and a short statement of motivation.
DEADLINE	**19 May 2026** · 23:59 CET
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