Computational/Experimental Symbiosis in the Design of Supramolecular Peptide Architectures

CSIC Consejo Superior de Investigaciones Científicas

Universidad del País Vasco · Euskal Herriko Unibertsitatea · CFM Materials Physics Center Centro de Física de Materiales

GOBIERNO DE ESPAÑA · MINISTERIO DE CIENCIA E INNOVACIÓN · AGENCIA ESTATAL DE INVESTIGACIÓN

CIC biomaGUNE MEMBER OF BASQUE RESEARCH & TECHNOLOGY ALLIANCE

EXCELENCIA MARÍA DE MAEZTU 07/2018 - 06/2022

Gipuzkoako Foru Aldundia · Ekonomia Sustapeneko, Landa Inguruneko eta Lurralde Orekako Departamentua

Diputación Foral de Gipuzkoa · Departamento de Promoción Económica, Medio Rural y Equilibrio Territorial

Ivan R. Sasselli,[1,2] Laura Perez-Chirinos,[2] Aitziber L. Cortajarena,[2,3] & Zaida Alvarez.[4]

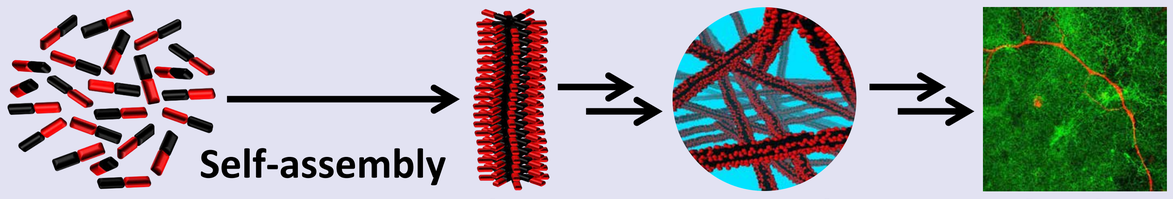
i.sasselli@csic.es

[1]**Materials Physics Center (MPC-CFM)**, CSIC-UPV/EHU, San Sebastian, Spain. [2]**CIC biomaGUNE**, Basque Research and Technology Alliance (BRTA),San Sebastian, Spain. [3]**Ikerbasque**, Basque Foundation for Science, Bilbao, Spain. [4]**Institute for Bioengineering of Catalonia (IBEC)**, Barcelona, Spain.

https://doi.org/10.17952/37EPS.2024.P1307

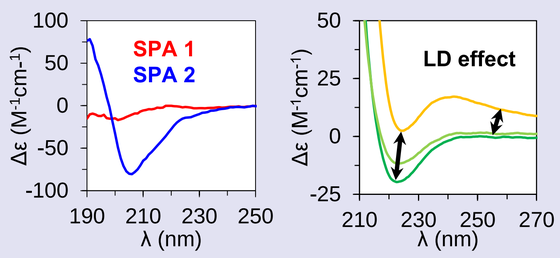
Supramolecular Peptide Assemblers (SPAs)

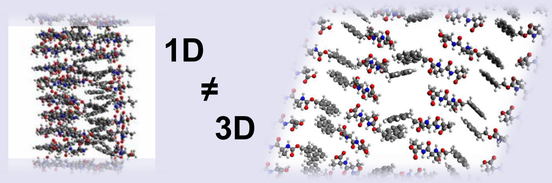
- Short peptides able to self-assemble into fibres[1]
- Form networks with excellent performance as artificial extracellular matrices (ECMs)[2]



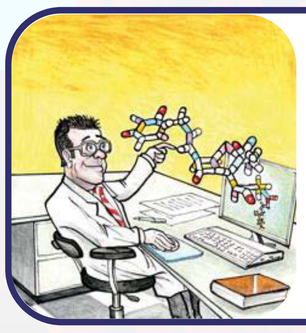
Design & Understanding Challenges

- Experimental characterization from proteins ➔ challenging interpretation





- Lack of representative crystal structures to benchmark experimental and computational methods

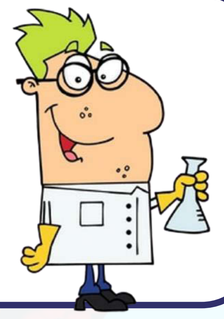


We propose: Computational/Experimental Symbiosis

- Computational work:
  - Improves experimental data interpretation
  - Gives intermolecular detail

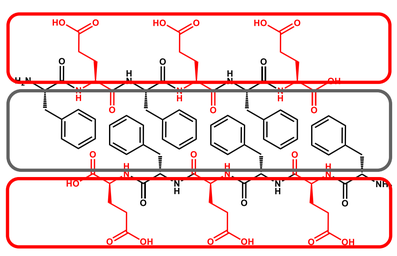
Side-by-side implementation
Continuous feedback
Iterative process

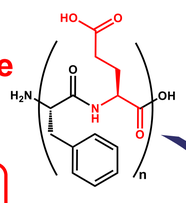
- Experimental work:
  - Starting and final point
  - Determines model set-up
  - Validates computational data



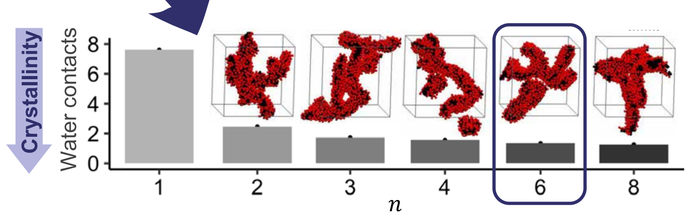
Amyloid Like Peptides (ALPs)

- $(FE)_n$ repeats:
  - Hydrophilic surface
  - Hydrophobic core



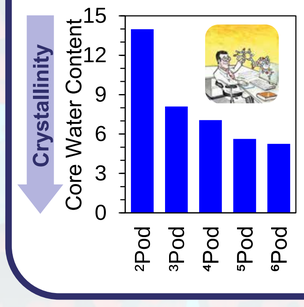


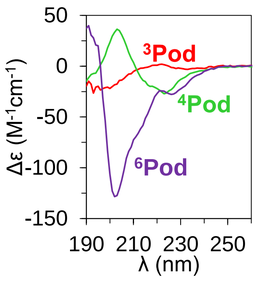
- Crystallinity prediction (effect of *n*)
- Converges ➔ *n = 6*

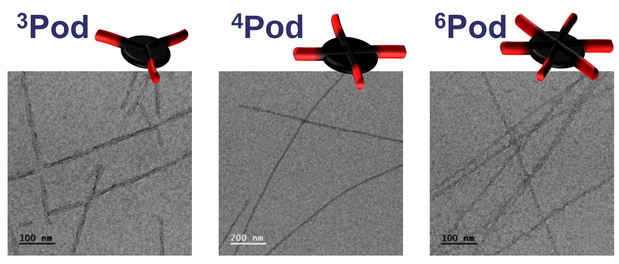


Short Branched Peptides (SBPs) ► nPods

- Branching in peptides ➔ hydrogen bonding patterns
- Number (*n*) of *Pods* determines order/cohesion

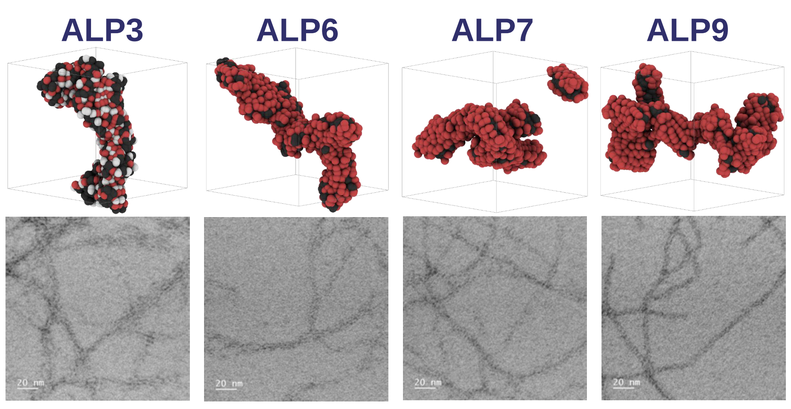




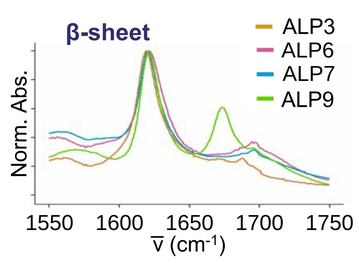


Charge Density Effect in Bioactivity

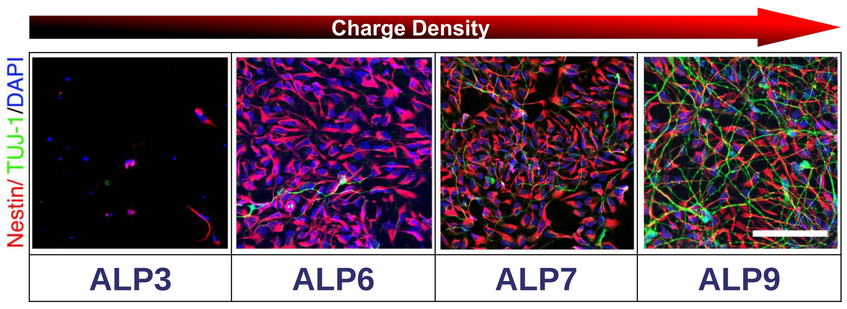
- Assess the effect of charge density on bioactivity
- ALP Library of Charges -3 to -9/peptide



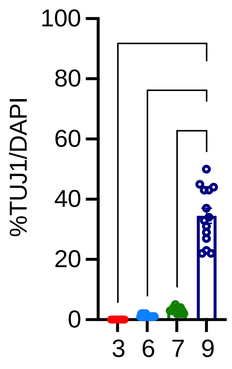
Fibres with strong intermolecular order



- Neuronal differentiation from Neuronal Progenitor Cells (NPCs)

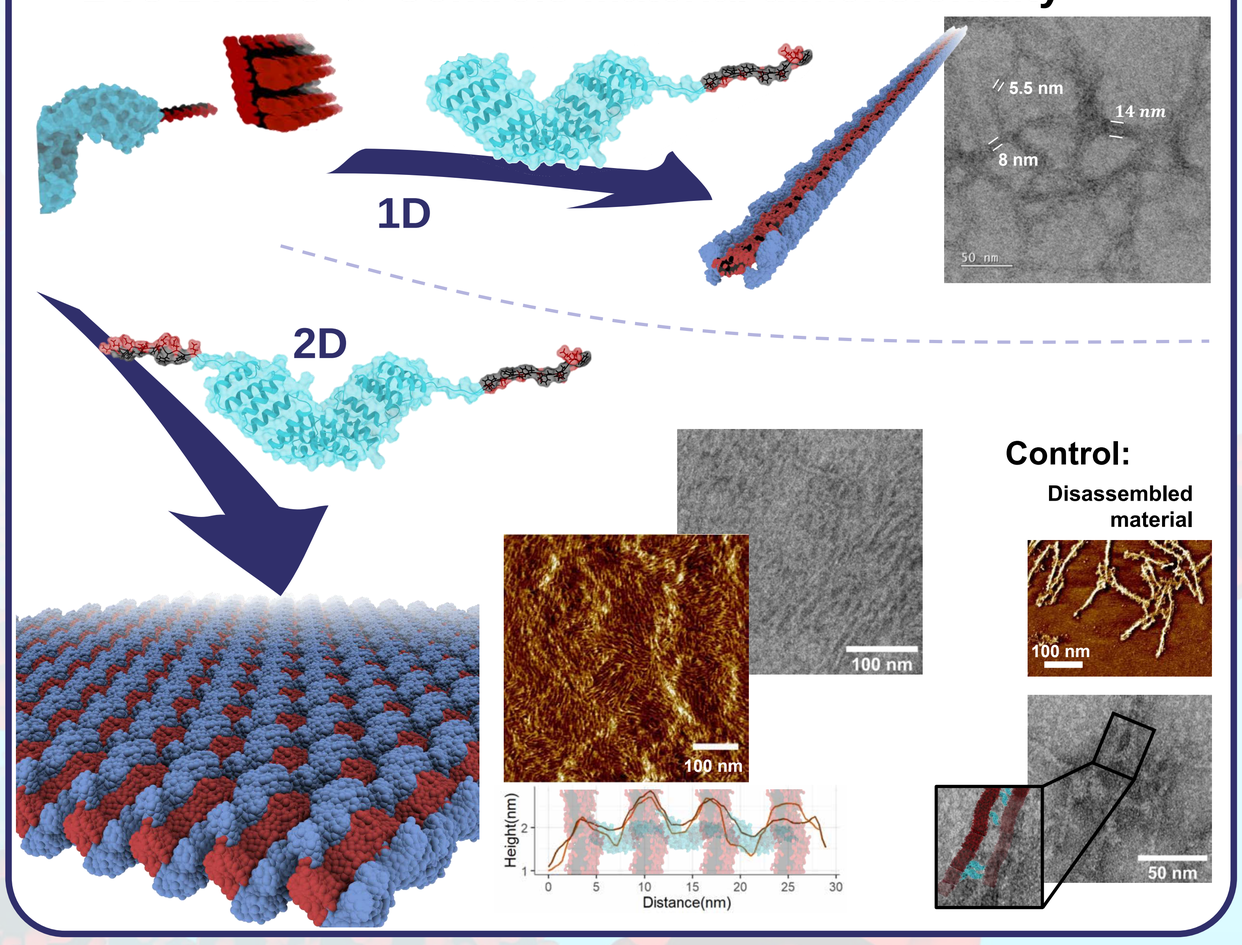


TUJ1= Neurons



Protein-ALP Hybrid Assemblies

- Tetratricopeptide Repeat (TPR) protein[3] + ALPs
- 1 *vs* 2 ALPs ➔ Controls material dimensionality



Conclusions

- nPod: new parameter to control intermolecular cohesion.
- ALP libraries: key role of charge density in the bioactivity of SPAs.
- Hybrid assemblies: control dimensionality and nanoscale morphology.
- ***The Computational/Experimental Symbiosis is a powerful approach to design materials with novel features and understand their function.***

References

1. Sasselli, Syrgiannis. *Eur. J. Org. Chem.* **2020**, *2020, 5305.*
2. Alvarez, Kolberg-Edelbrock, Sasselli, Stupp *et al. Science*, **2021**, *374*, 848.
3. Cortajarena, Sasselli, *et al. Acc. Chem. Res.* **2021**, *54*, 3836.

Acknowledgements

- Ramon y Cajal (RYC2021-033294-I)
- Gipuzkoa Fellow (2019-FELL-000017-01)
- Maria de Maeztu Units of Excellence (MDM-2017-0720)