Amyloid-inspired biomaterials: present and future

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INTRODUCTION

The amyloid state is commonly associated with various neurodegenerative diseases, but there are also functional amyloids involved in biological processes. Amyloid fibers possess properties such as mechanical strength and self-assembly, which are of interest for the development of bioinspired materials. Applications will be explored in the environmental, biomedical, and biosensor development fields, including structures such as hydrogels, nanospheres, and fibers, to better understand the potential of these technologies and the benefits they can bring in terms of sustainability, health, and technology.

OBJECTIVES

- To change the general association of amyloid proteins with pathogenesis
- To showcase various amyloid-inspired materials and applications
- To describe the main structural characteristics of the amyloid state
- To explore the challenges and opportunities of amyloid-inspired materials

STRUCTURAL CHARACTERISTICS AND FIBRILLIZATION MECHANISM

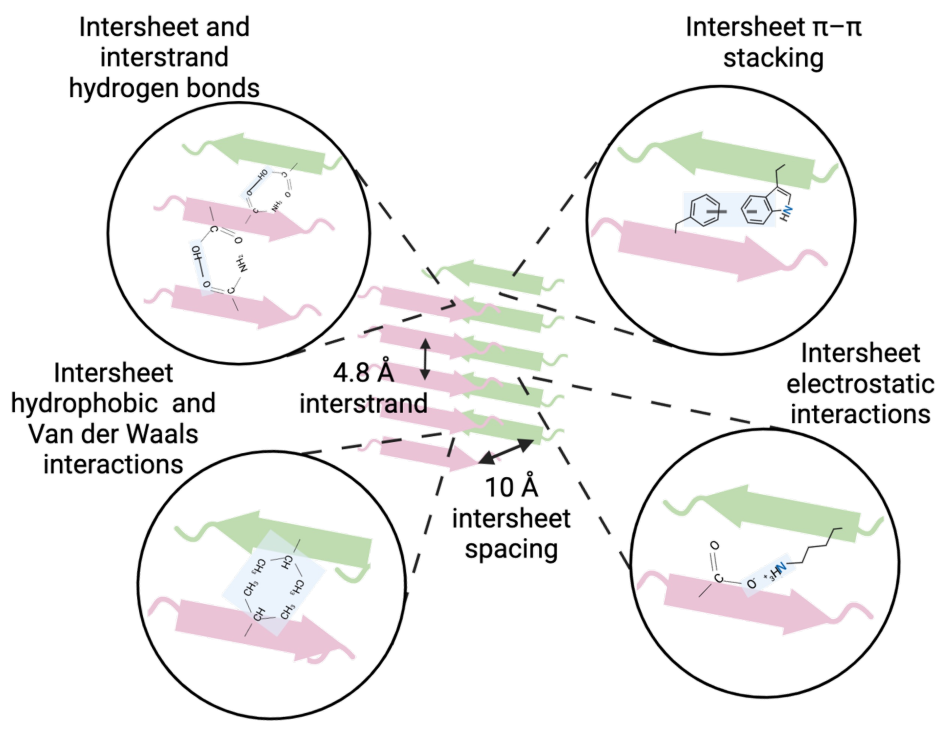


Figure 1: Scheme of non-covalent interactions in amyloid fibers.

The protein's sequence and physiological functions are not critical factors in the formation of amyloid structures.

Amyloid aggregates consist of a motif of parallel or antiparallel β-sheets that fold through different non-covalent interactions. [1]

This remarkably stable structure confers resistance to heat, a broad pH range, and proteases, highlighting its potential implications for bio-inspired materials.

The formation of amyloid fibers is a complex process involving multiple intermediate stages.

A few protein monomers come together to form oligomers, which act as aggregation nuclei for the growth of amyloid protofibrils through the addition of more monomers. Formed protofibrils can interact between them and form fibrils.

This process can be catalyzed by introducing "seeds", which reduces the latency phase. [2]

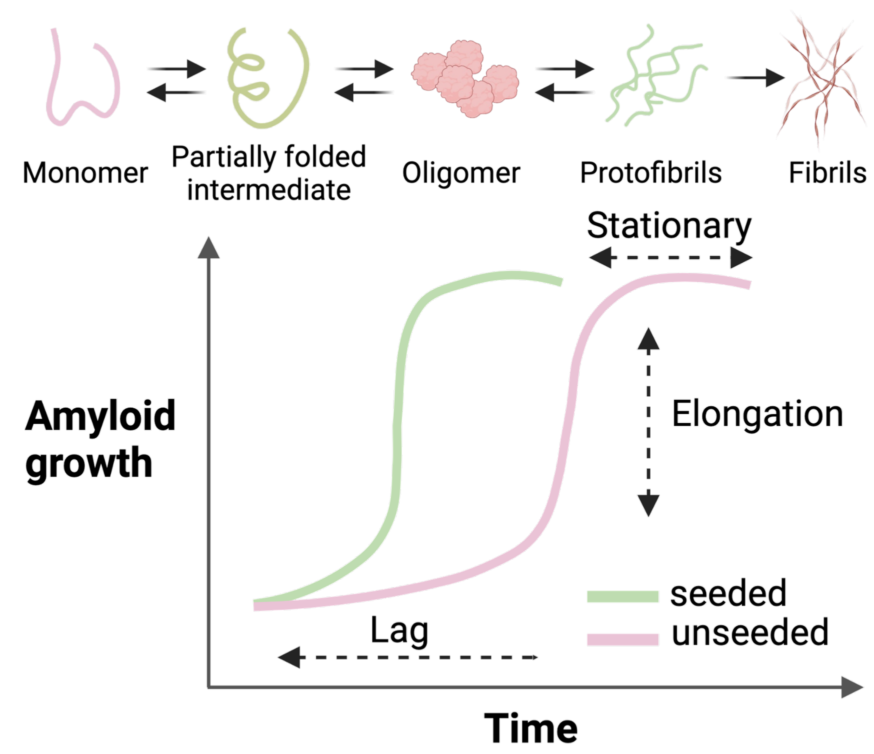


Figure 2: Fibrillization process' scheme and kinetics.

APPLICATIONS OF BIOINSPIRED MATERIALS IN AMYLOID STRUCTURES

Biosensor generation
Nanofibers

Amyloid fibers as an alternative to costly compounds in electrochemical sensors (A, B).

Engineering an octapeptide derived from adenovirus fibrous protein (NS) to incorporate a cysteine for coordination bonding with copper ions (C, black).

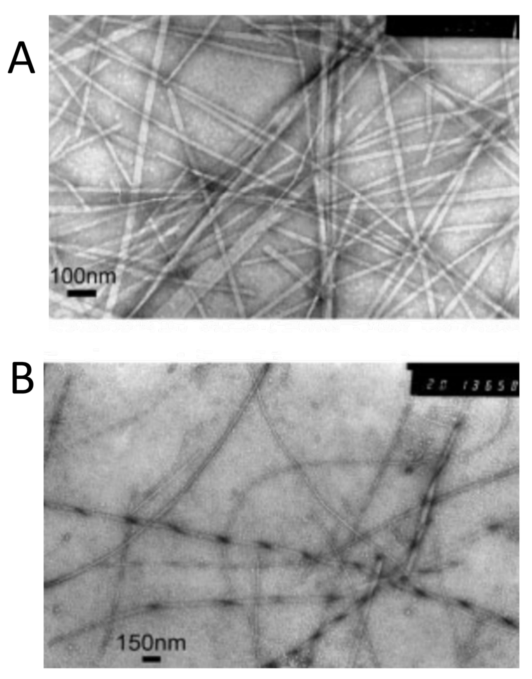
The aggregation process is facilitated by non-covalent interactions of the constant region (C, red).

Nanofibers are deposited onto gold electrodes (D).

Regeneration of fibers for repeated use + mild synthesis conditions.

On-site detection of copper in solution.

Practical applications in diagnosing disorders related to copper metabolism. [3]



C

Peptide	Sequence
NS (original)	N-S-G-A-I-T-I-G
NC	N-C-G-A-I-T-I-G
CN	C-N-G-A-I-T-I-G
CS	C-S-G-A-I-T-I-G

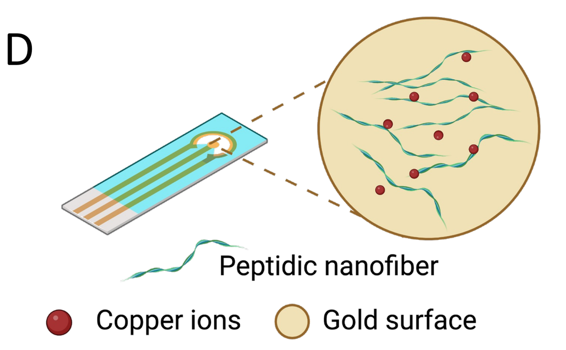


Figure 3: TEM images of fibrils (A,B), peptide sequences (C) and scheme of the technology.

Environmental Remediation
Aerogel

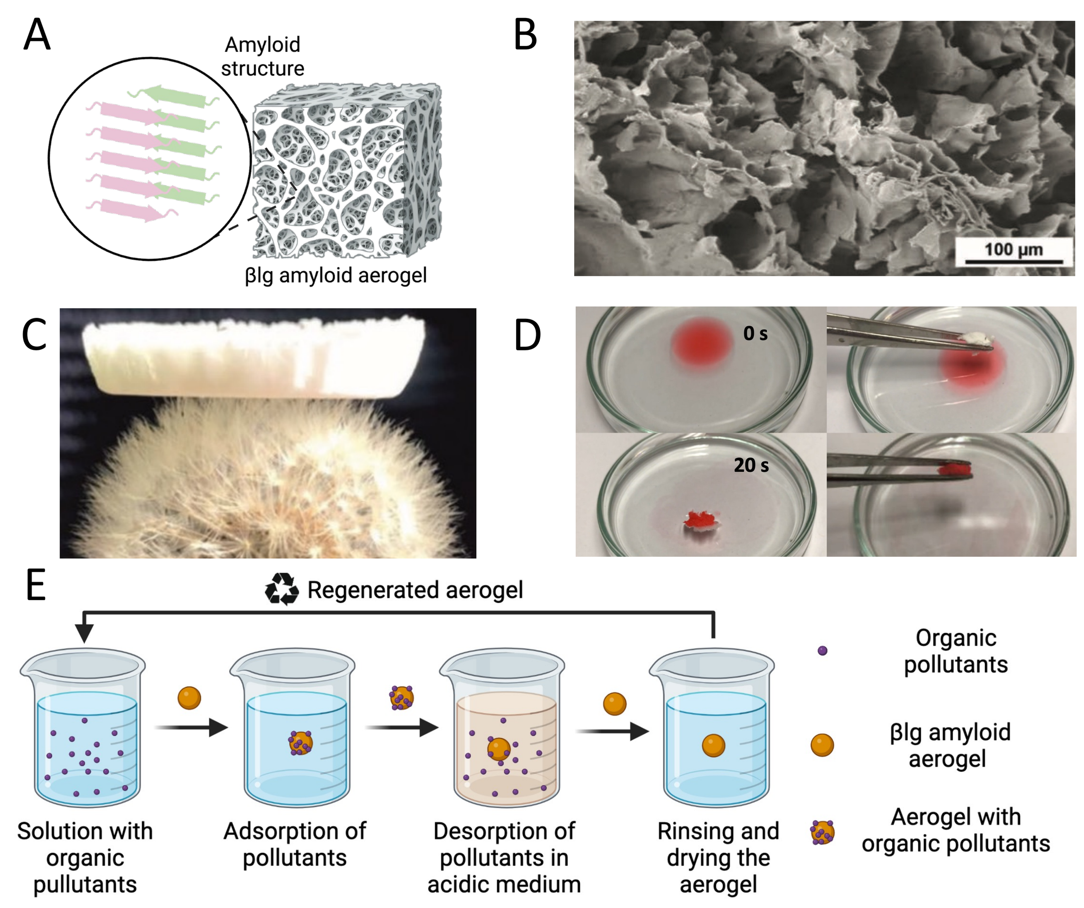


Figure 4: Scheme of aerogel's structure (A), TEM image of the aerogel (B), aerogel's high adsorption capacity and lightweight demonstration (C,D) regeneration process (E).

Amyloid fiber-based aerogels as a novel way for water purification (A).

Use of β-lactoglobulin (βlg) to generate lightweight and highly porous aerogels with remarkable adsorption capacity for organic pollutants (B-D).

Regeneration of aerogels through acid washing to enhance adsorption performance (E).

Environmentally friendly solution and cheap, as βlg is a byproduct of dairy industry. [4]

Biomedical field
Spherical nanoparticles

Amyloid structure-based approach for addressing the COVID-19 pandemic by preventing the interaction between ACE2 receptor and Spike's RBD of SARS-CoV-2 (A).

Spherical nanoparticles generated from an amyloid core (red) fused with DHFR protein (grey) and an oligomer with high affinity towards RBD of S protein [LCB1 and LCB2] (blue) (B).

Stability of the constructs under various conditions and absence of cytotoxic effects.

Advantages of spontaneous assembly, scalability, and stability at room temperature.

Suitability for prophylactic and diagnostic applications and modification to target other viruses.[5]

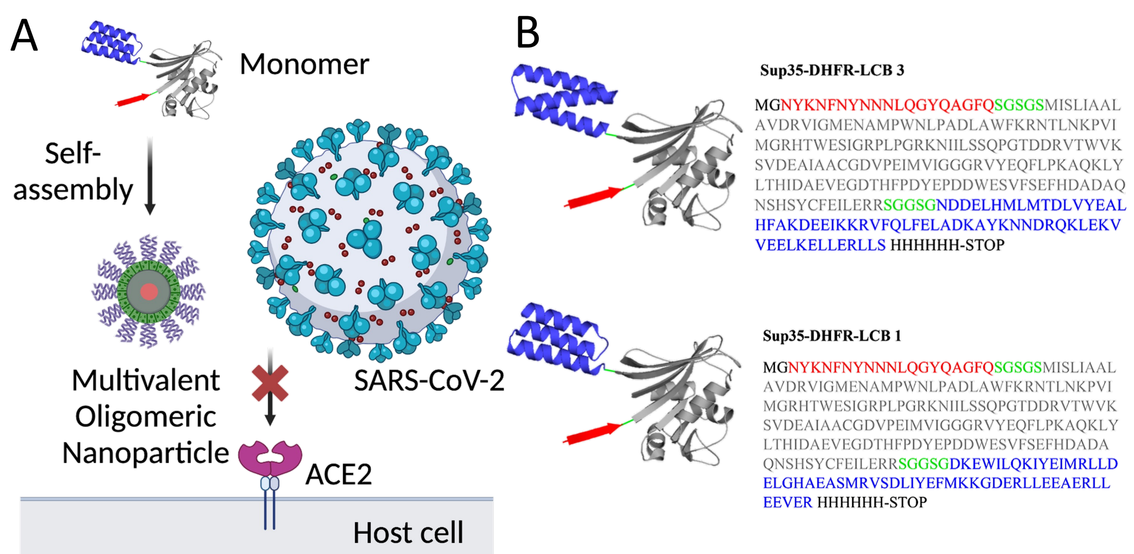


Figure 5: Scheme of the blockage of the interaction between SARS-CoV-2 and host's ACE2 receptor by the amyloid nanoparticles (A). Structure and sequence of OligoBinders (B).

CHALLENGES, OPORTUNITIES AND CONCLUSIONS

- Amyloids peptides have attractive properties and potential applications due to their structure, functionality, versatility, and biocompatibility.
- Controlling their self-assembly is challenging but crucial for specific applications, requiring the development of strategies to direct this process.
- AI combined with molecular dynamics software can aid in understanding amyloid protein behavior.
- Environmental impact should be considered, and sustainable sources like byproducts or plant-derived proteins can also be taken into consideration.
- Biocompatibility balance is crucial, considering the potential risks associated with amyloid diseases.
- Demonstrating long-term safety is essential to overcome negative perceptions.

METHODOLOGY

The study utilized a methodology involving systematic literature search and bibliographic synthesis. Relevant information was gathered from existing studies and publications to inform the research findings. Figure shaping in Biorender to summarize and represent the information.

REFERENCES

[1] Lai, Y; et al. "Bio-inspired amyloid polypeptides: From self-assembly to nanostructure design and biotechnological applications." Applied Materials Today, Volume 22, March 2021. **[2] Mankar, S.; et al.** "Nanomaterials: amyloids reflect their brighter side." Nano Rev. 2, 10.3402/nano.v2i0.6032. May 2011 **[3] Viguier, B.**; et al. "Development of an Electrochemical Metal-Ion Biosensor Using Self-Assembled Peptide Nanofibrils." ACS Appl. Mater. Interfaces 2011, 3, 5, 1594–1600. **[4] Peydayesh, M.; et al.** "Amyloid Fibrils Aerogel for Sustainable Removal of Organic Contaminants from Water." Advanced Materials, Volume 32, Issue 12, 06 February 2020 **[5] Behbahanipour, M.; et al.** "OligoBinders: Bioengineered Soluble Amyloid-like Nanoparticles to Bind and Neutralize SARS-CoV-2." ACS Appl Mater Interfaces, 2023 Mar 8;15(9):11444-11457.