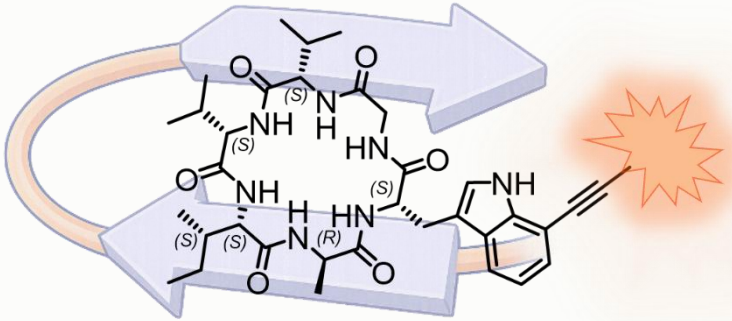
Cyclopeptide-Based Fluorescent Probes for Monitoring Prefibrillar Aβ42 Nanostructures

Steven Panek

PhD Candidate

Bielefeld University, Germany · Université Paris-Saclay, France

https://doi.org/10.17952/38EPS.2026.O49



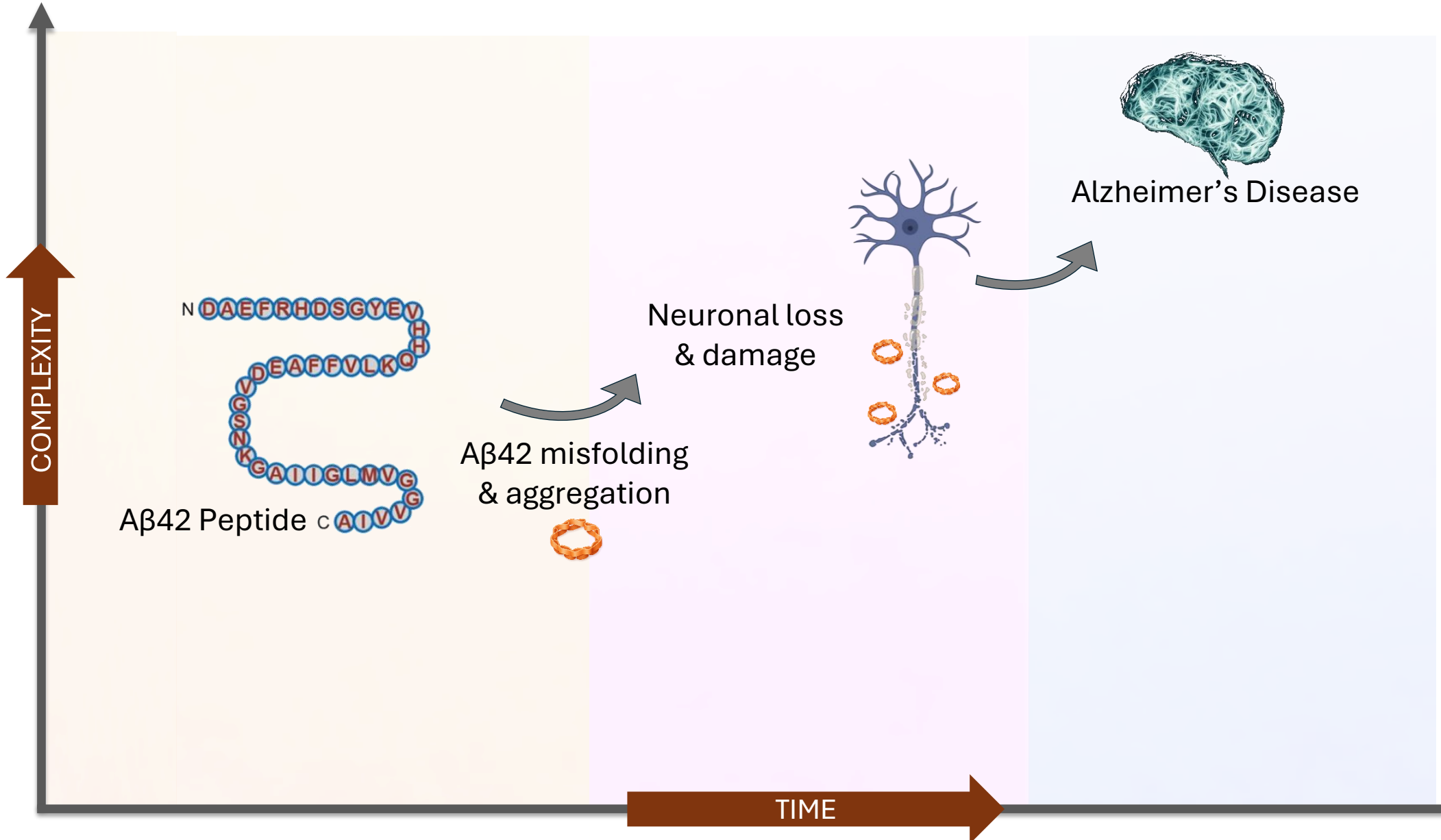
Research conducted in

Norbert Sewald Group
Bielefeld University

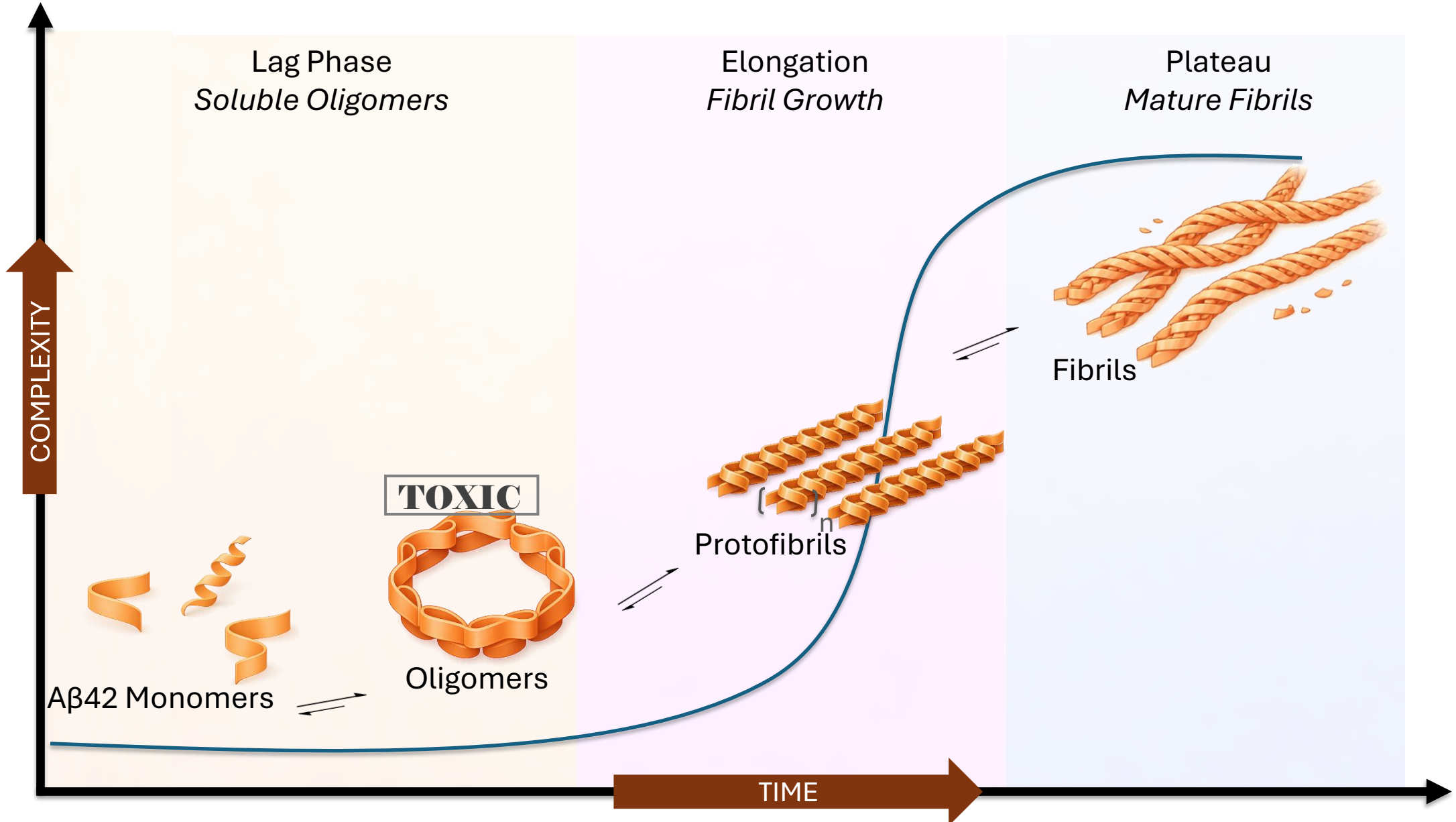
Nicolò Tonali Group
CEA Paris-Saclay

38th European Peptide Symposium
Vienna, Austria · September 9, 2026

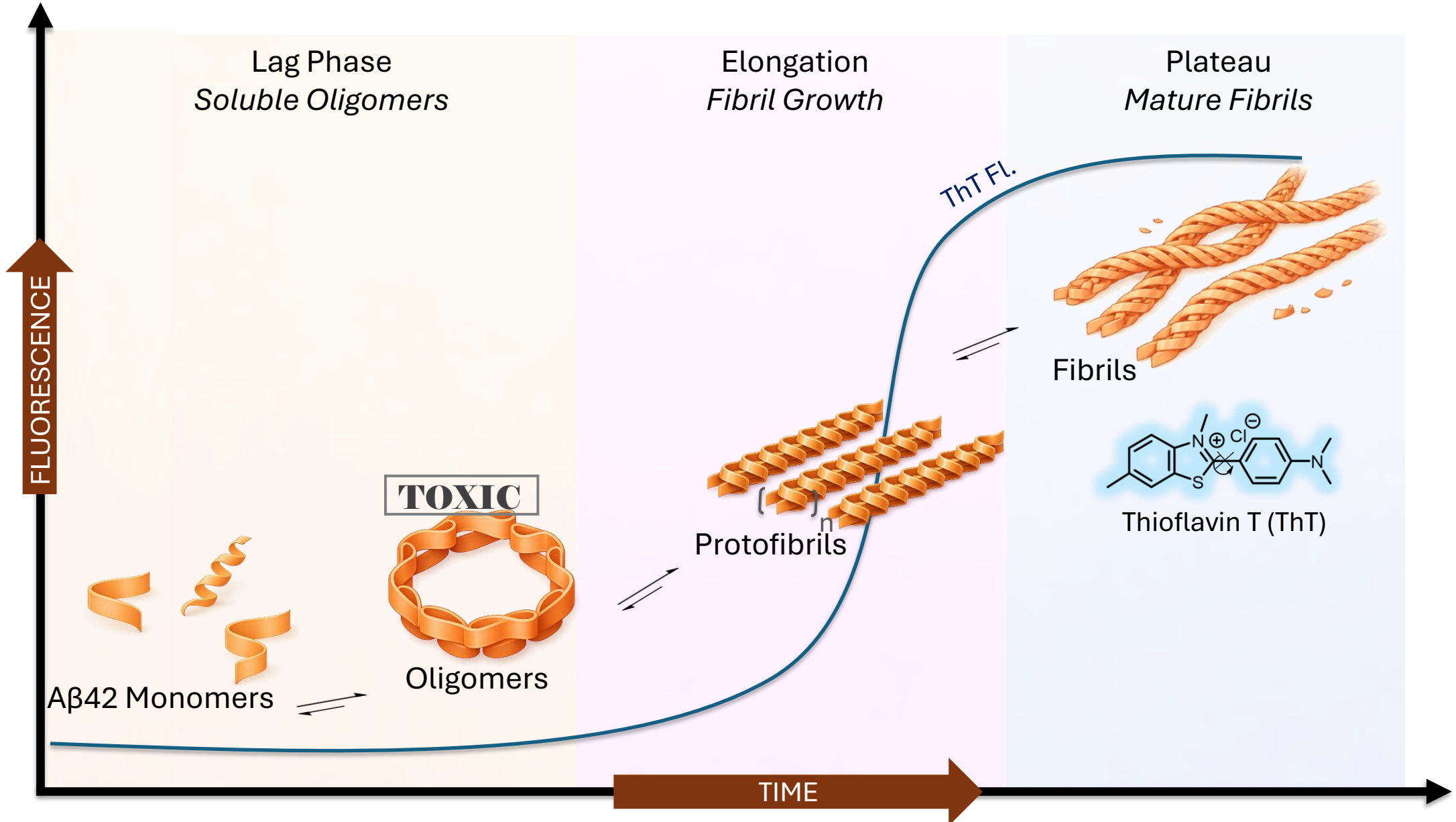
Aβ42 Misfolding in Alzheimer's Disease



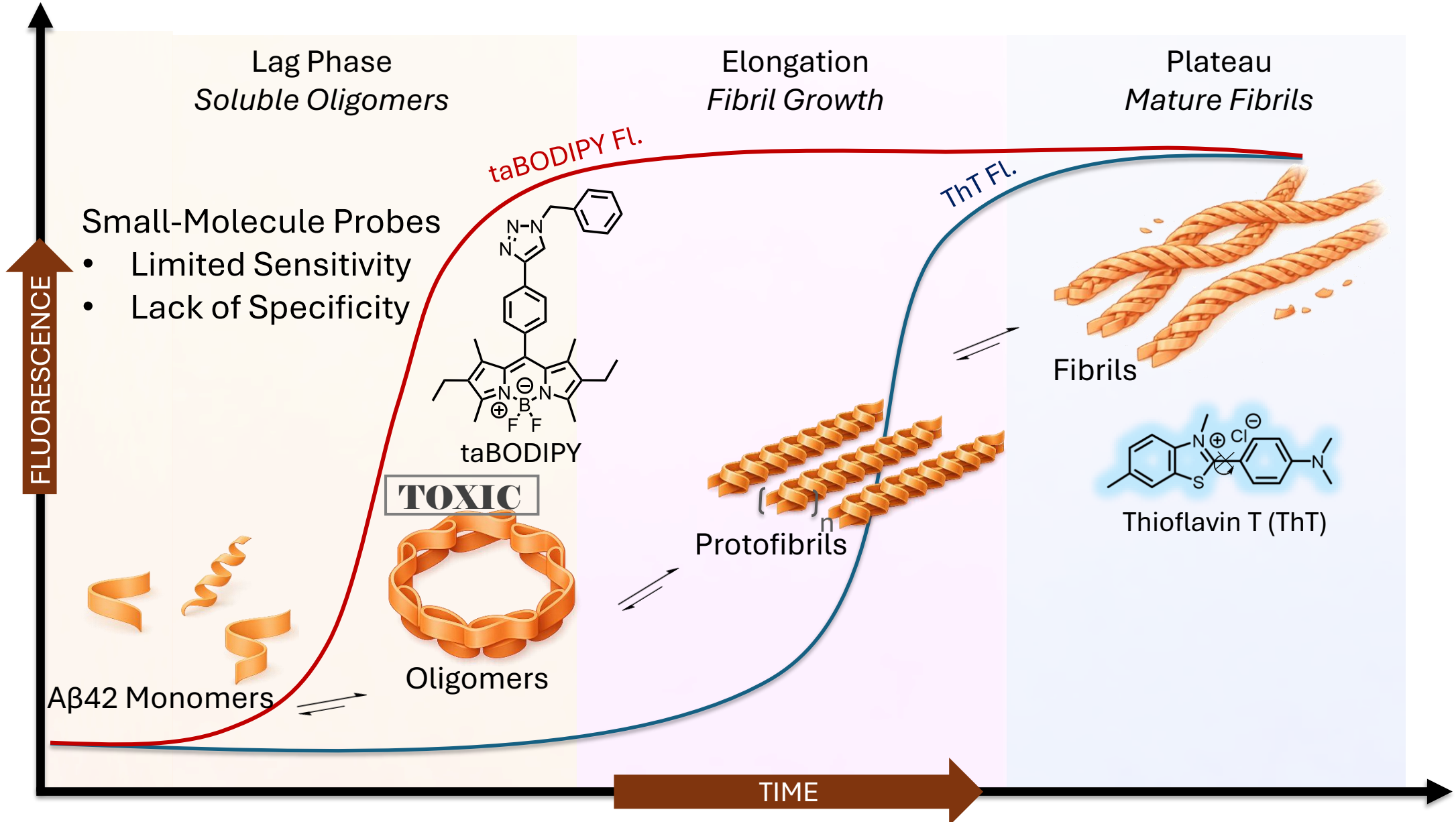
Aβ42 Aggregation Pathway



Aβ42 Aggregation Pathway

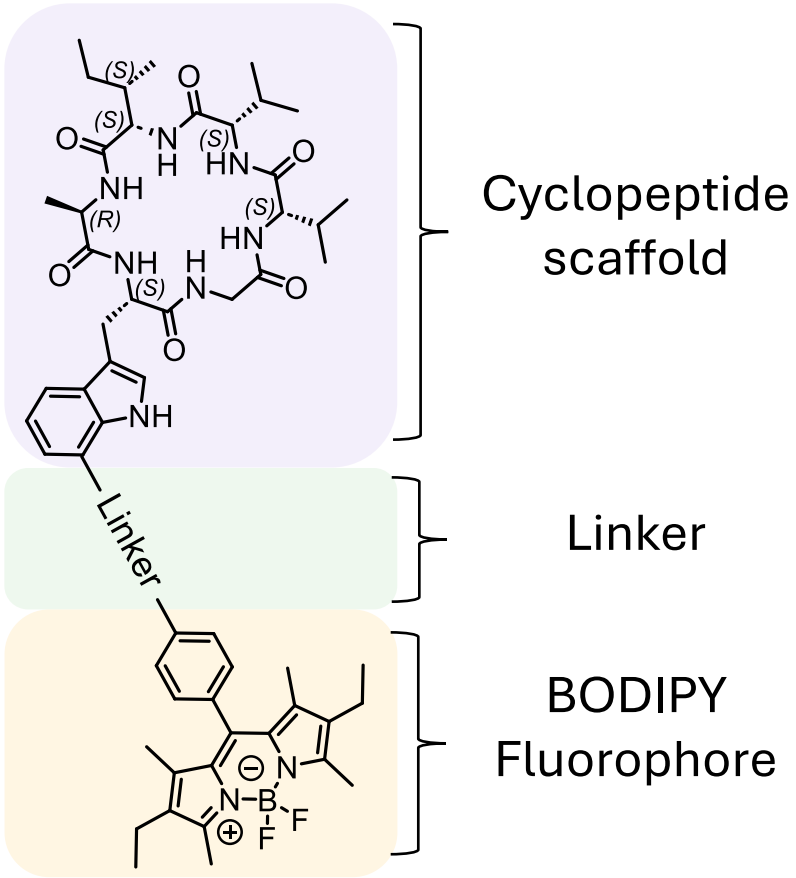


Aβ42 Aggregation Pathway



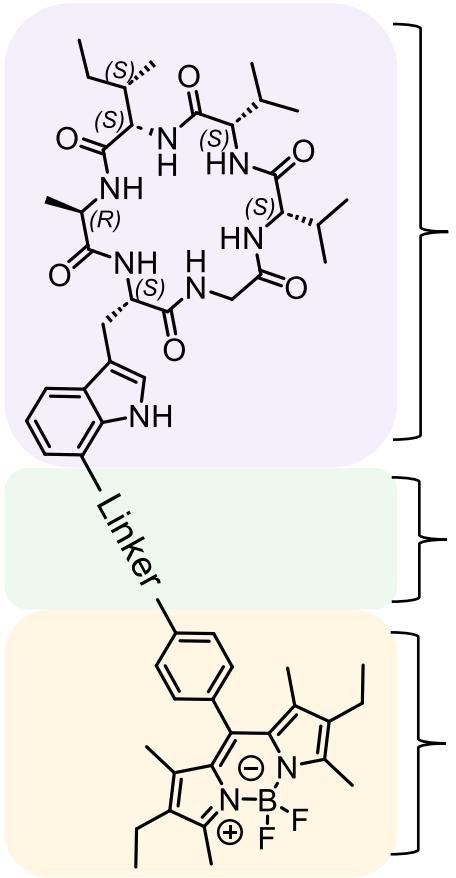
Design of Peptide-Fluorophor-Conjugate

Probe Architecture



Hypothesis: Aβ42 Oligomer Detection

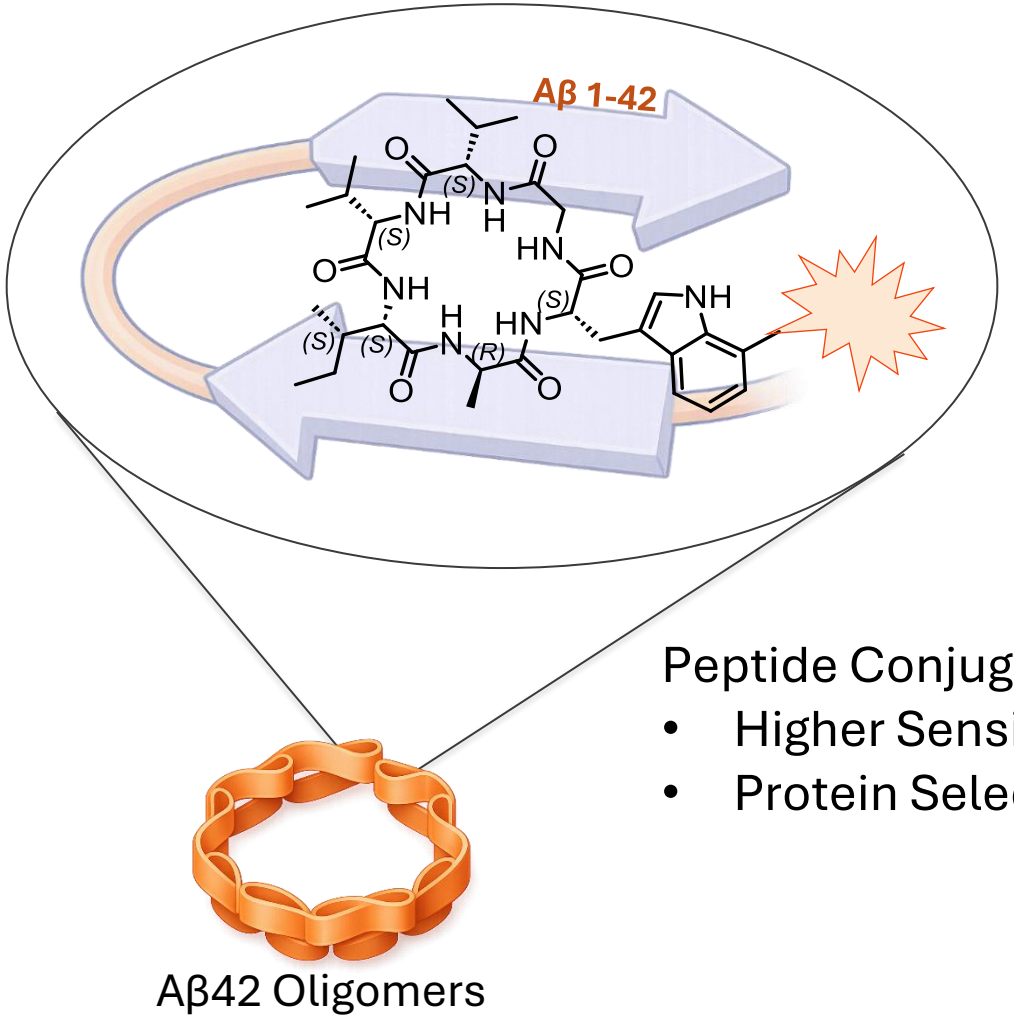
Probe Architecture



Cyclopeptide scaffold

Linker

BODIPY Fluorophore



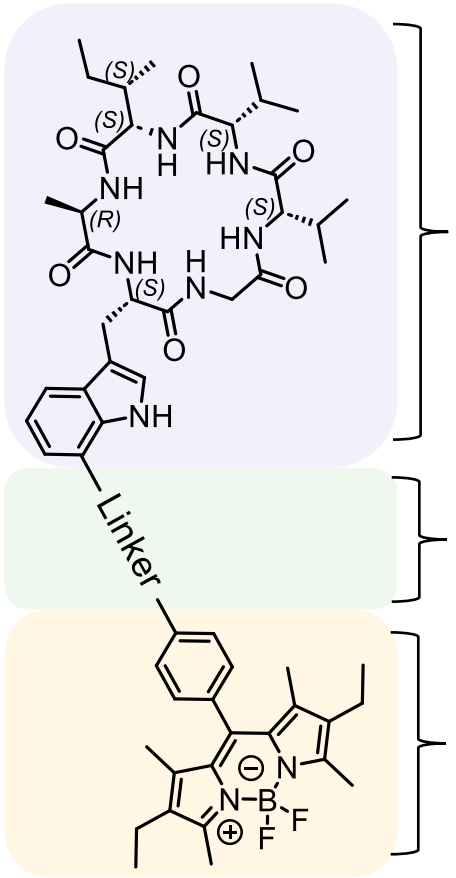
Aβ42 Oligomers

Peptide Conjugate Probes:

- Higher Sensitivity?
- Protein Selectivity?

Hypothesis: Aβ42 Oligomer Detection

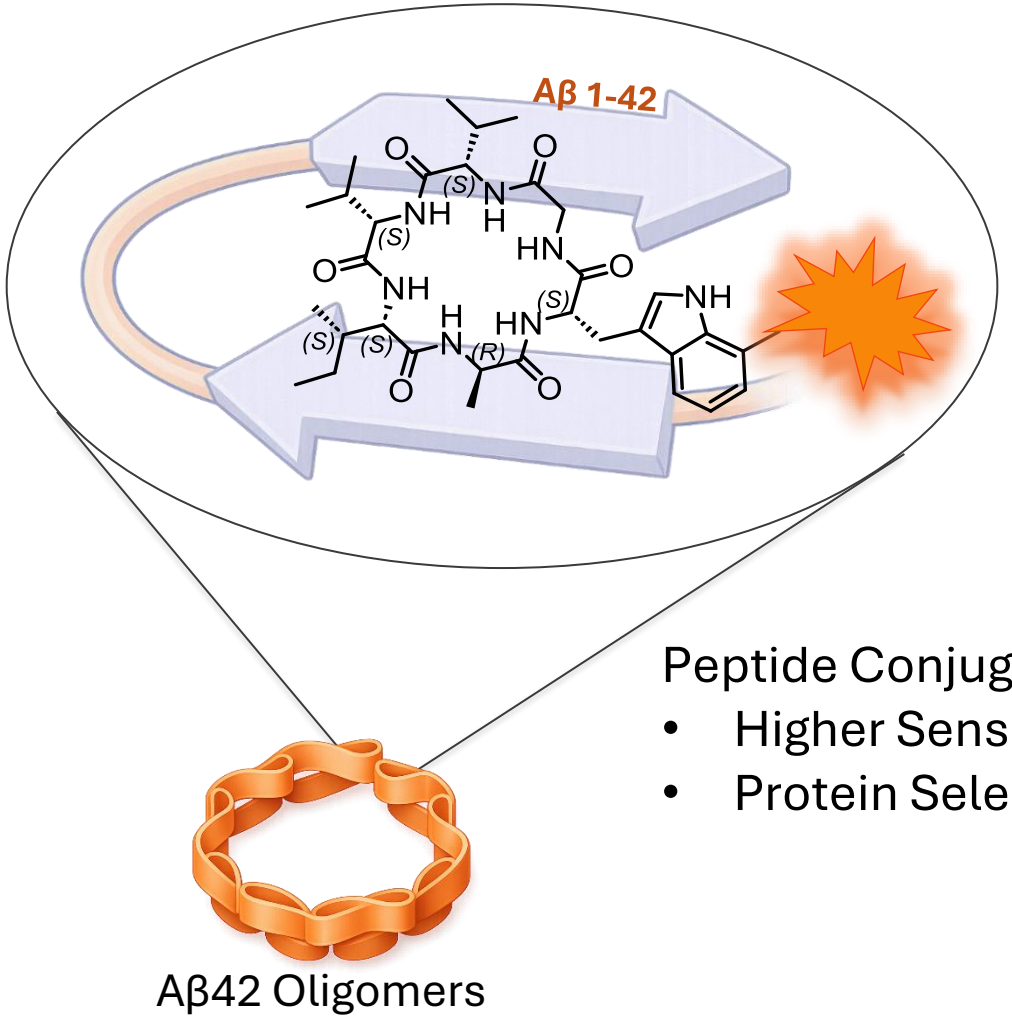
Probe Architecture



Cyclopeptide scaffold

Linker

BODIPY Fluorophore



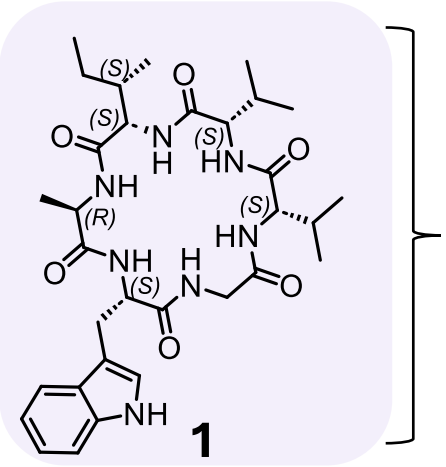
Aβ42 Oligomers

Peptide Conjugate Probes:

- Higher Sensitivity?
- Protein Selectivity?

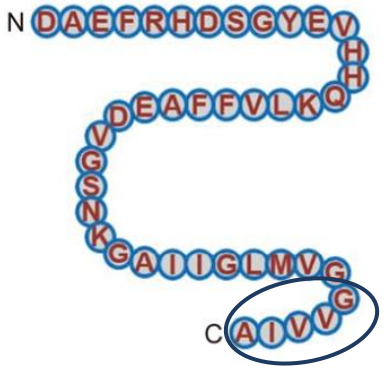
Cyclopeptide Design & Characterization

Probe Architecture



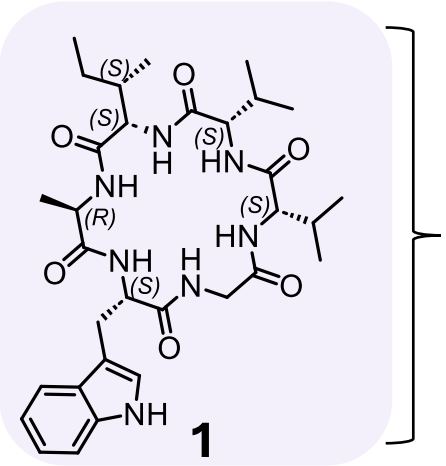
c(G[38]VVIa[42]W)

Aβ1-42 Sequence



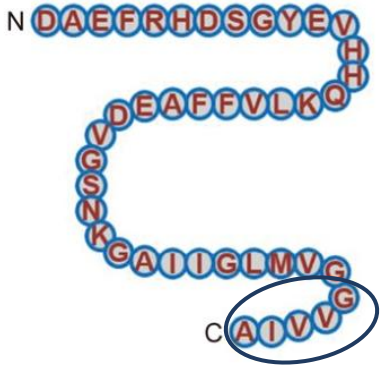
Cyclopeptide Design & Characterization

Probe Architecture

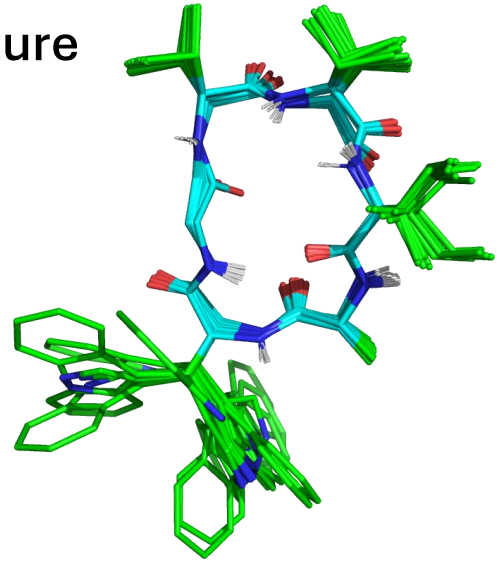


c(G[38]VVIa[42]W)

Aβ1-42 Sequence



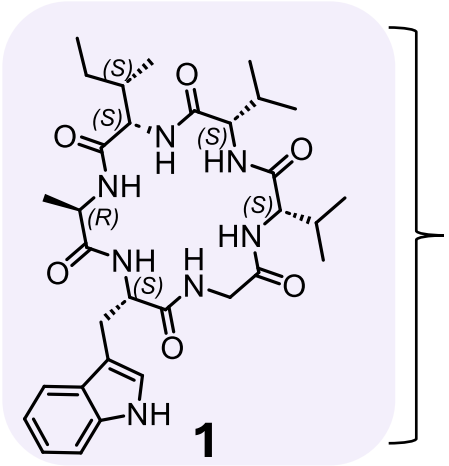
NMR Structure



- Well-Defined Confromation

Cyclopeptide Design & Characterization

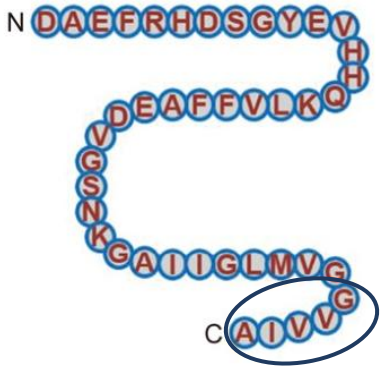
Probe Architecture



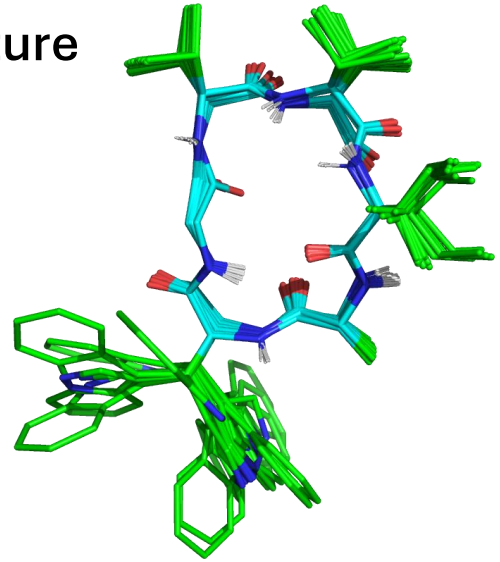
c(G^{38}VVIa^{42}W)

- Well-Defined Confromation
- No Interference with Aβ Aggregation

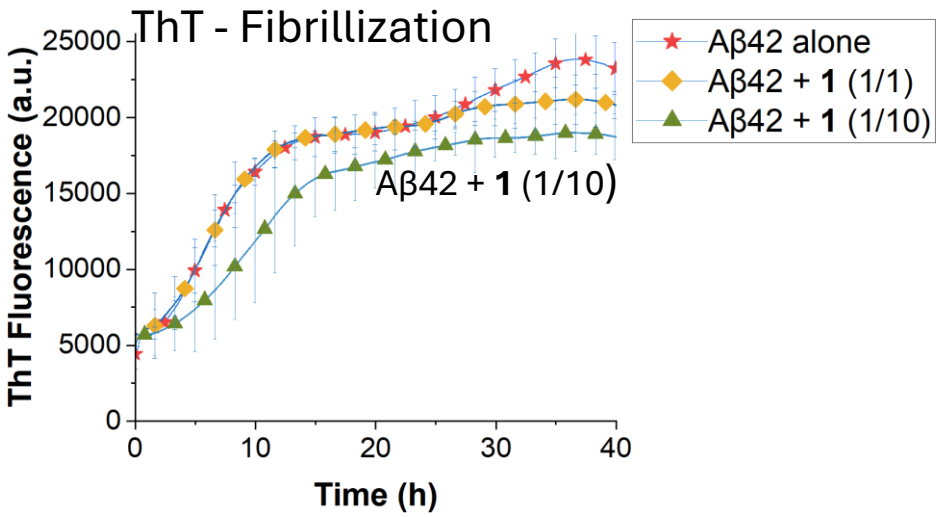
Aβ1-42 Sequence

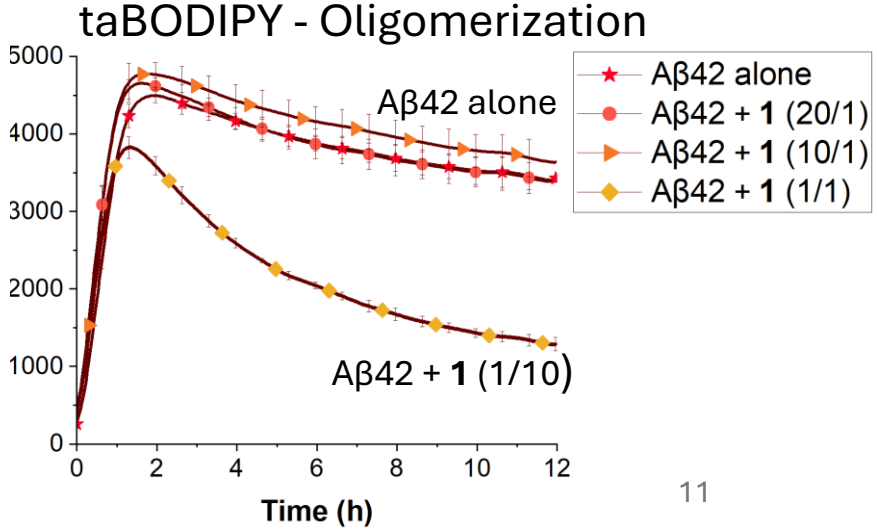


NMR Structure



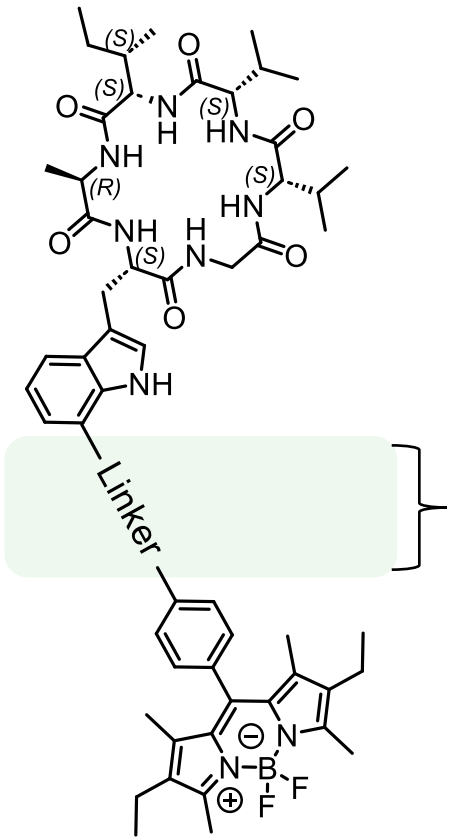
Effect on Aβ42 Aggregation



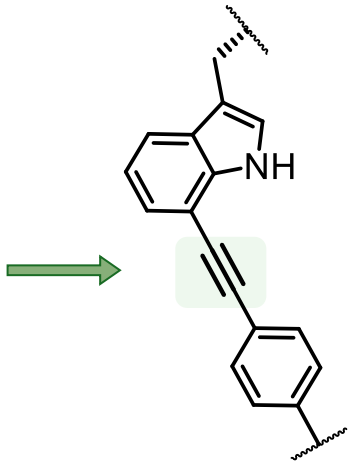


Design of Peptide-Fluorophor-Conjugate

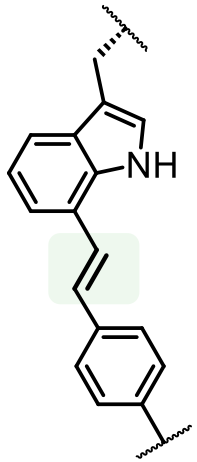
Probe Architecture



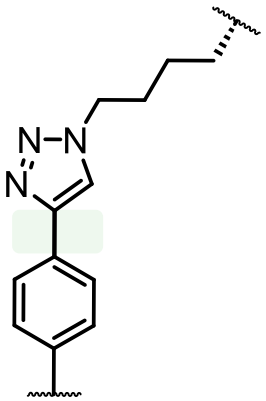
Linker



Rigid



Semi-flexible

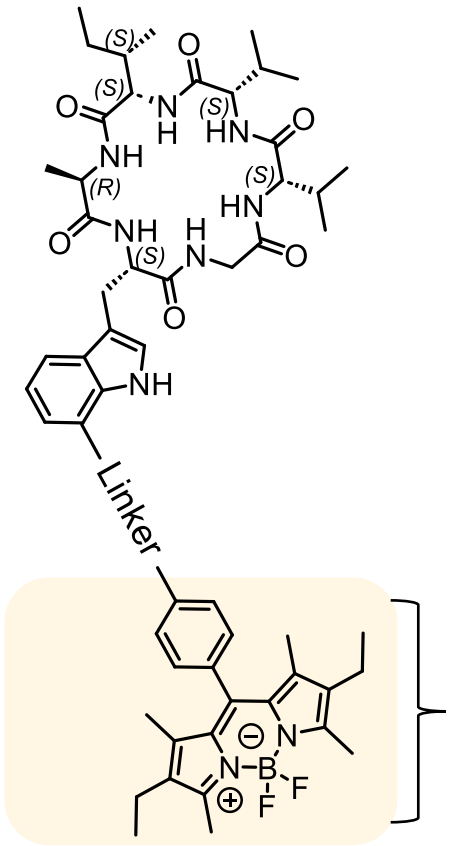


Flexible

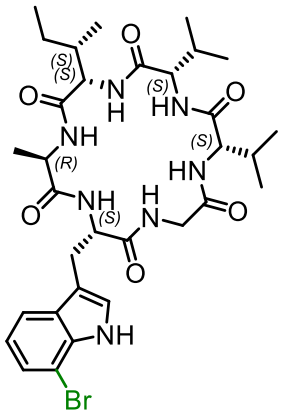
Increasing Linker Flexibility

Design of Peptide-Fluorophor-Conjugate

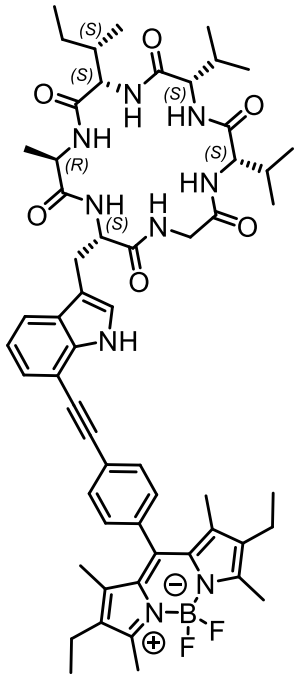
Probe Architecture



BODIPY
Fluorophore



Cross Coupling

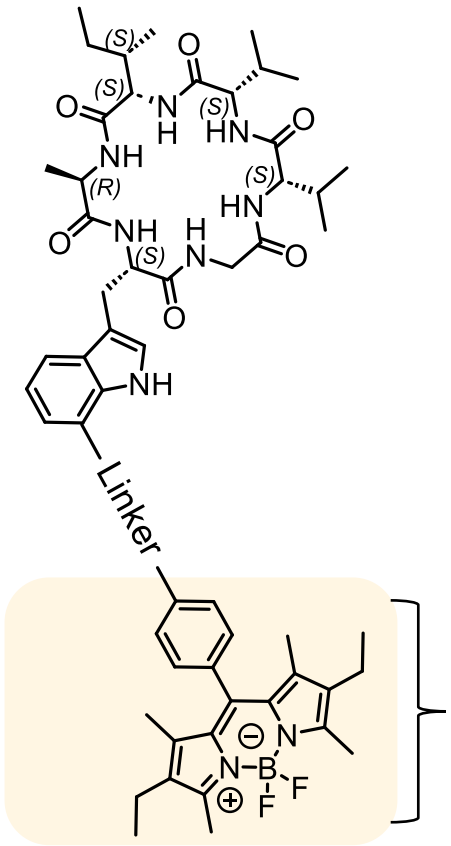


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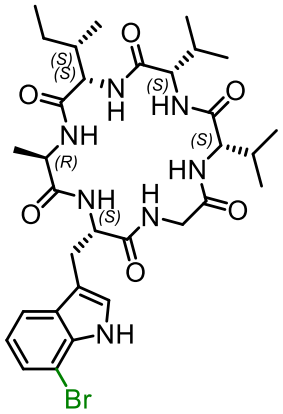
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Design of Peptide-Fluorophor-Conjugate

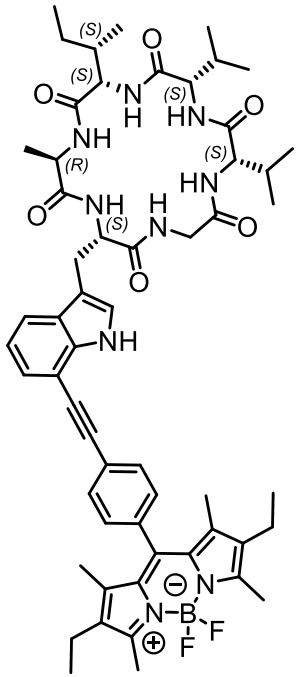
Probe Architecture



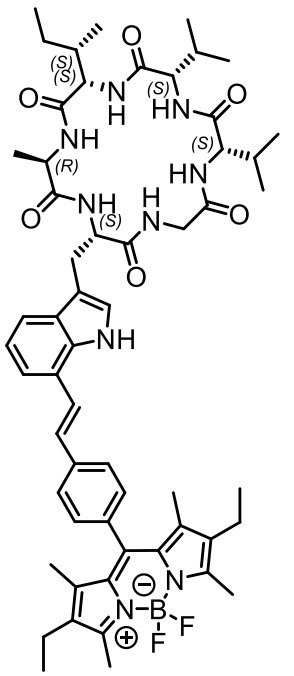
BODIPY
Fluorophore



Cross Coupling

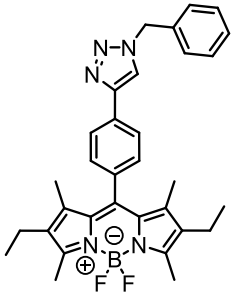


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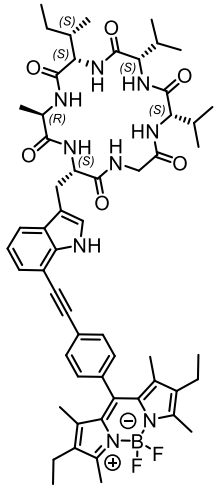


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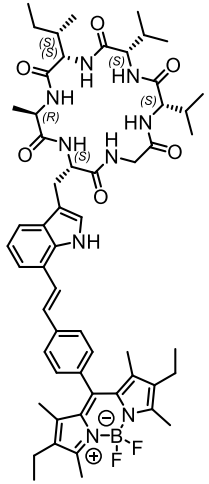
Probe–Linker Architectures



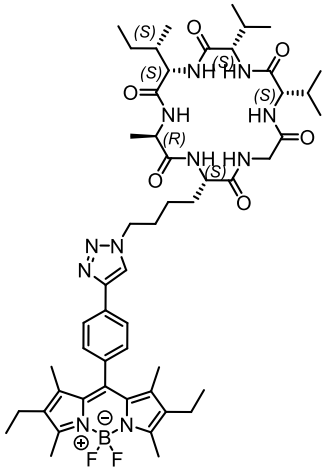
taBODIPY
Reference probe



2

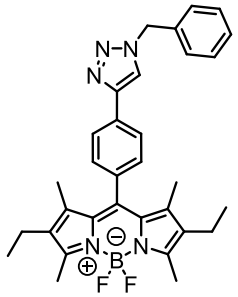


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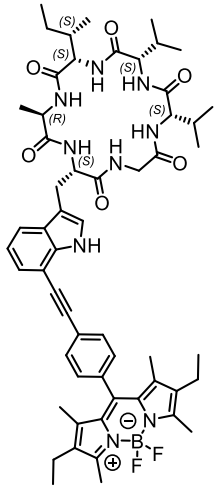


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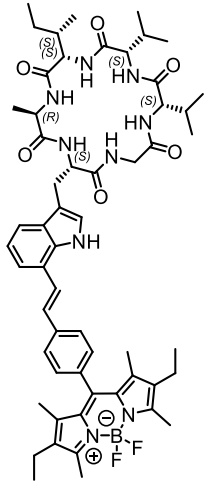
Aβ42 Detection



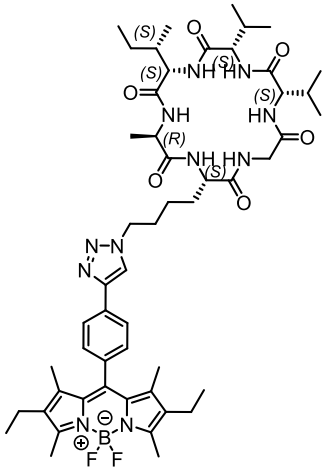
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Reference probe



2

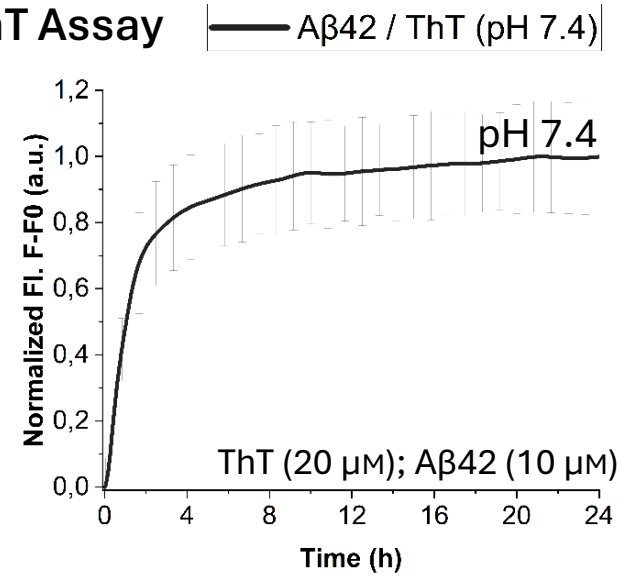


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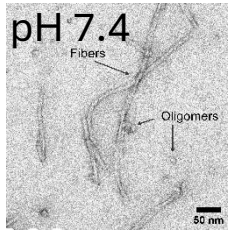


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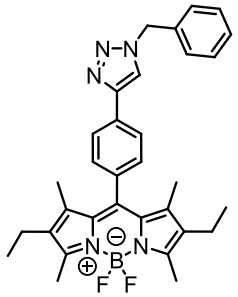
ThT Assay



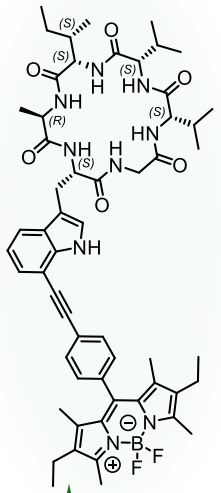
TEM, 24h



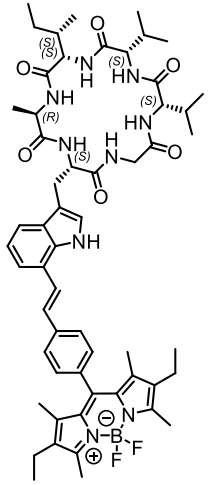
Aβ42 Detection



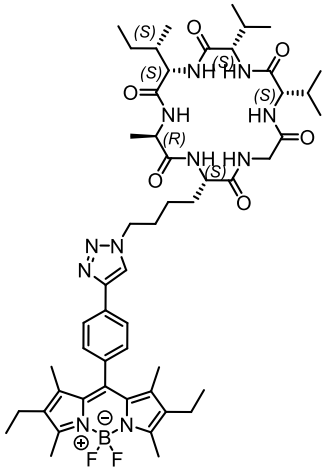
taBODIPY
Reference probe



★2

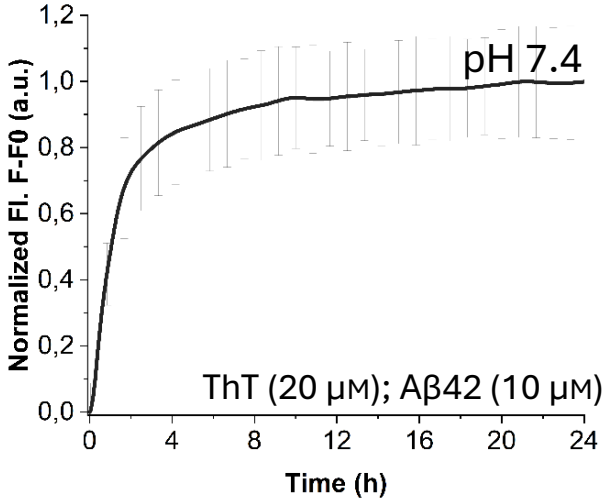


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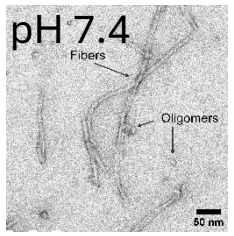


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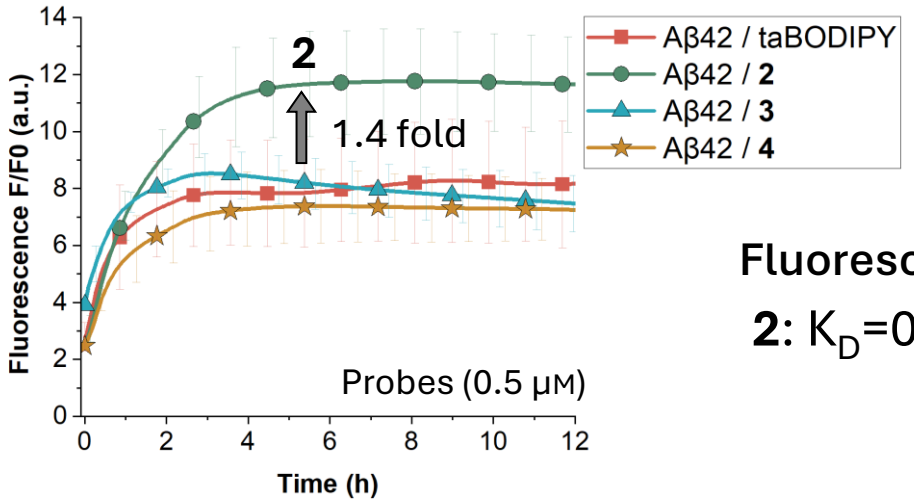
ThT Assay — Aβ42 / ThT (pH 7.4)



TEM, 24h



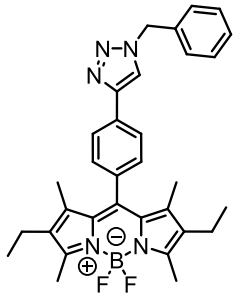
Probe Assay (pH 7.4)



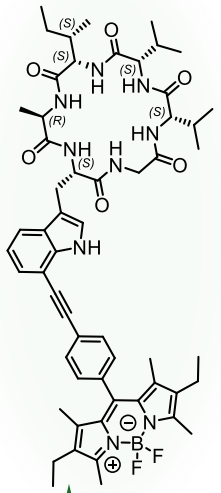
Fluorescence Titration

2: K_D=0.07 ± 0.04 μM

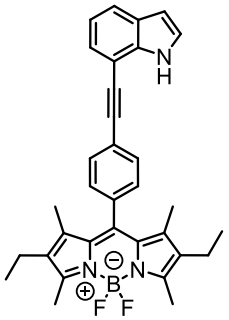
Aβ42 Oligomer Detection



taBODIPY
Reference probe



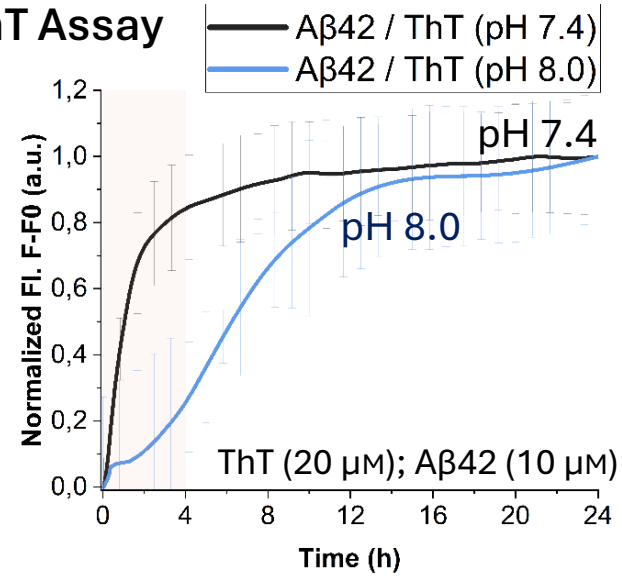
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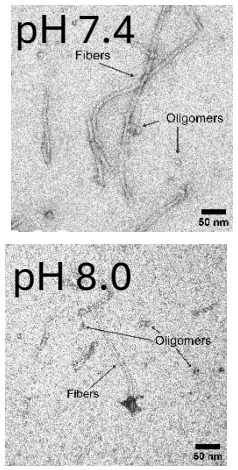
control (**5**)

- Sensitive Detection of Aβ1–42 Oligomers

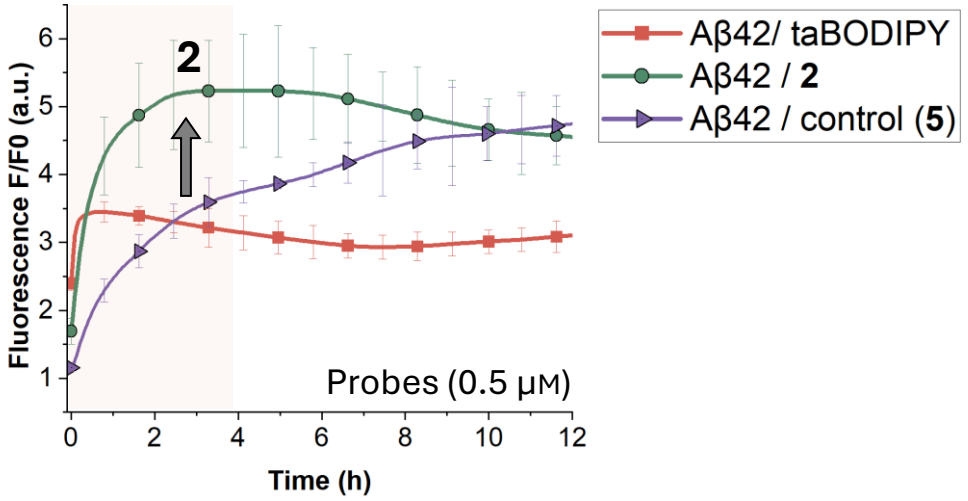
ThT Assay



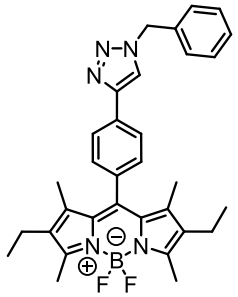
TEM, 24h



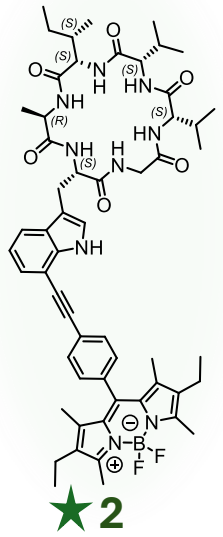
Probe Assay (pH 8.0)



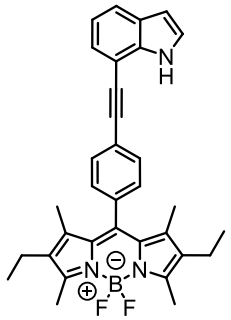
Selective Aβ42 Detection over IAPP



taBODIPY
Reference probe



★2



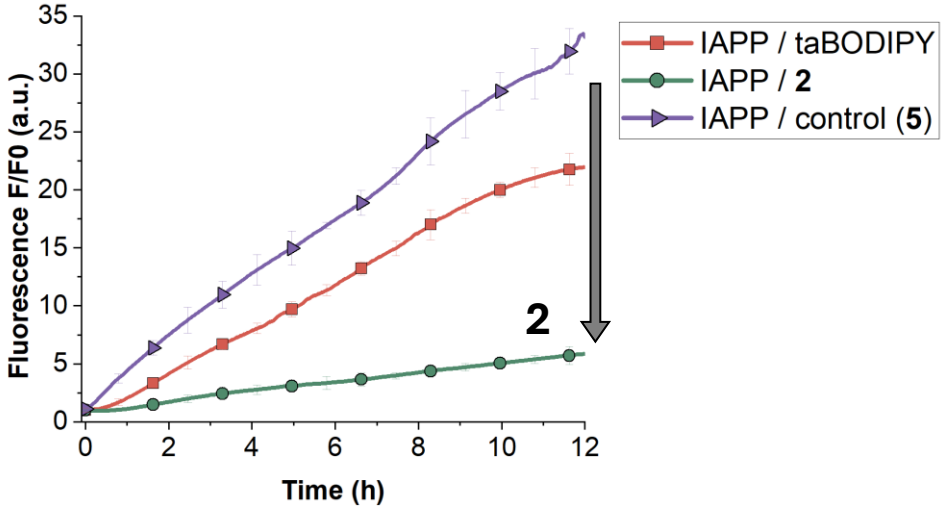
control (**5**)

- Sensitive Detection of Aβ1–42 Oligomers
- Aβ42 Selectivity over IAPP

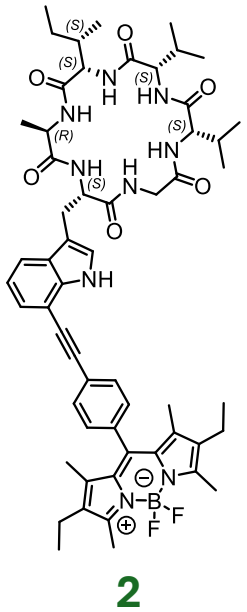
IAPP (Amylin)

- 37-Residue Amyloidogenic Peptide
- Linked with Diabetes Type 2

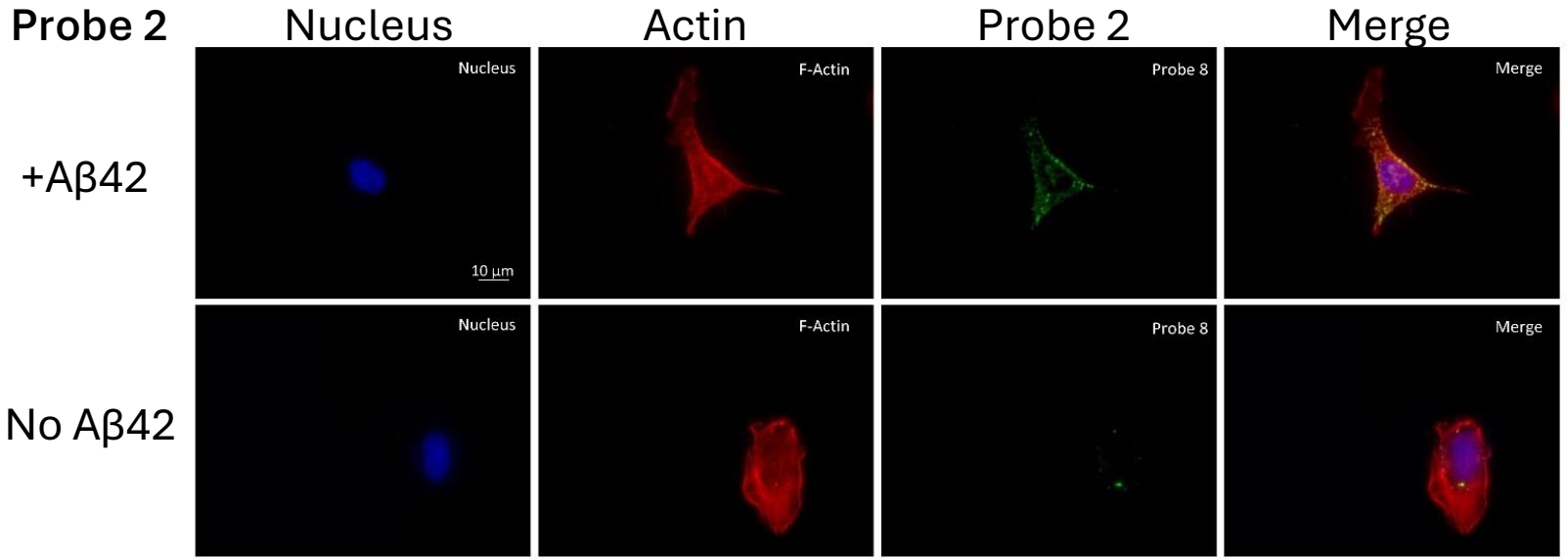
IAPP Assay



Cellular Aβ42 Oligomer

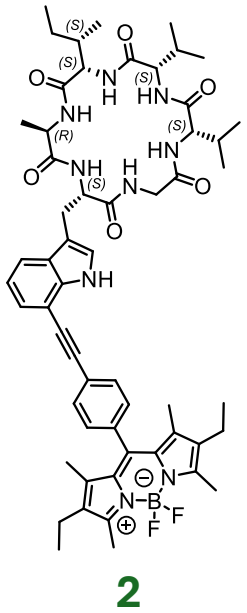


2

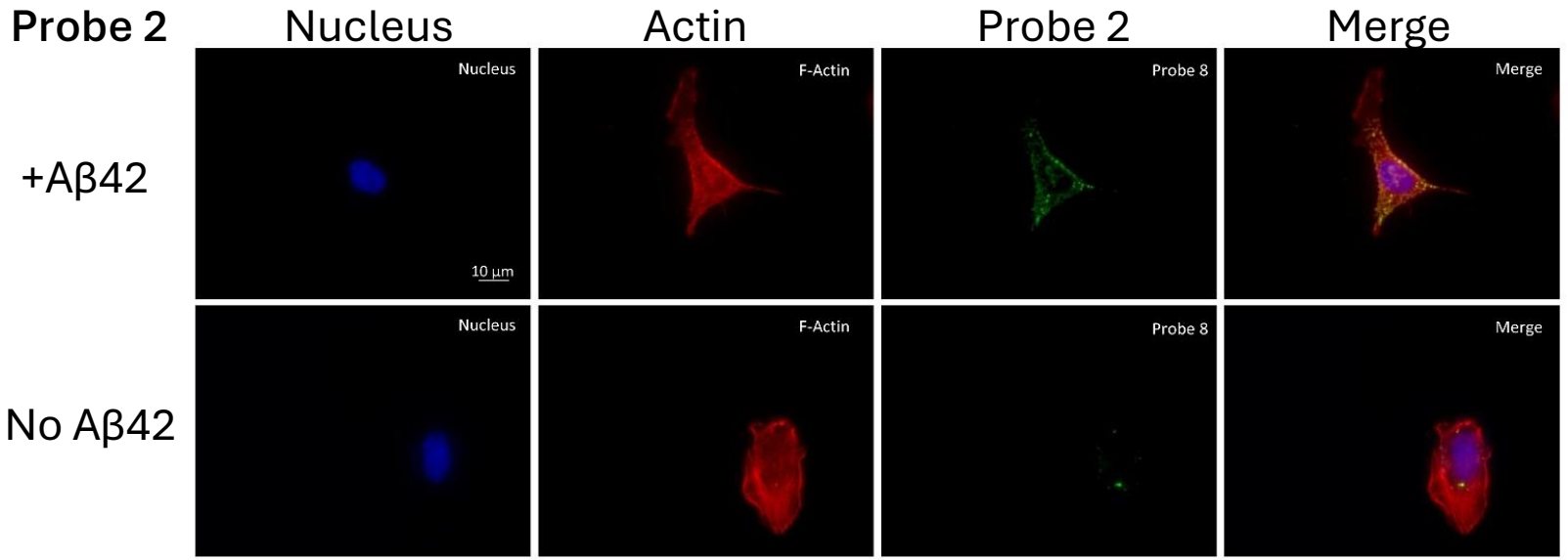


S. Panek et al., J. Med. Chem. 2026; 69 (6): 7377-7392.

Summary



2



Take-Home Message:
Peptide-based probes enable sensitive and selective detection of Aβ42 oligomerization.

S. Panek et al., J. Med. Chem. 2026; 69 (6): 7377-7392.

THANK YOU!

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Interested in a post-doc collaboration..?

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