

Tracking Of Amyloid- β Aggregation Transitions And Inhibitor Effects By FOPPR Binding Kinetics

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Abstract

Background:

Amyloid- β (A β) self-assembly generates structurally heterogeneous intermediates whose kinetics are linked to toxicity and therapeutic response in Alzheimer's disease.

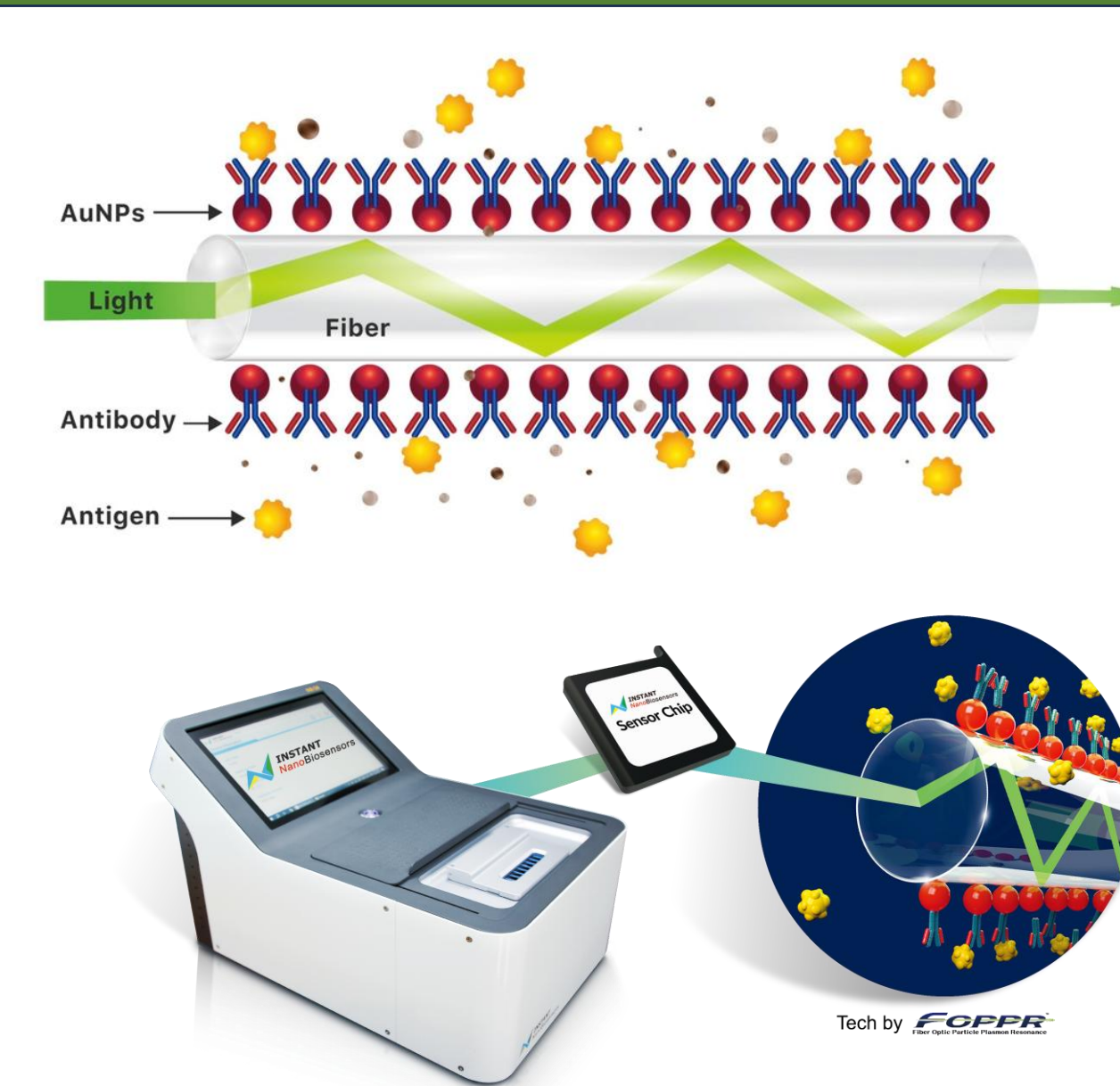
Objective:

We investigated whether epigallocatechin gallate (EGCG) modulates A β 42 aggregation in a concentration- and time-dependent manner.

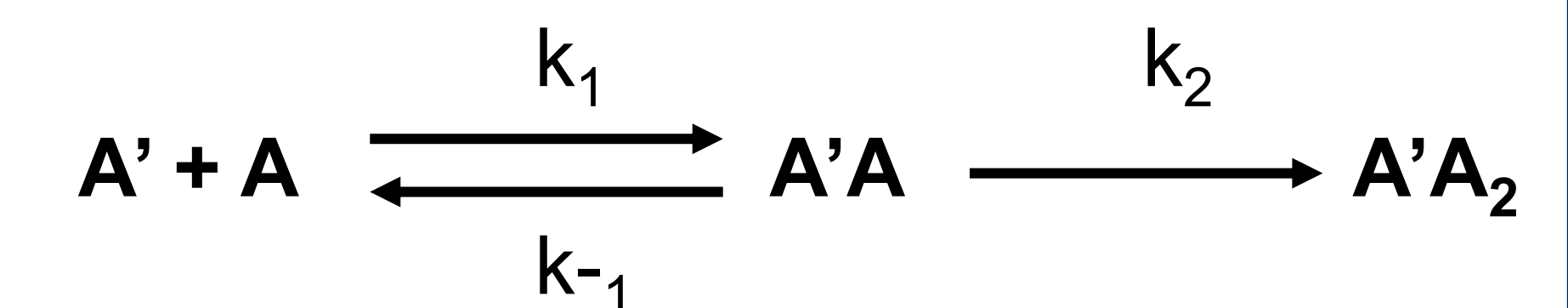
Methods

1) FOPPR Principle

Fiber Optic Particle Plasmon Resonance (FOPPR) was used as a rapid, label-free method to analysis aggregation-state transitions and inhibitor effects.



2) Kinetic Model



Association: $A' + A \rightleftharpoons A'A$

Elongation: $A'A \rightarrow A'A_2$

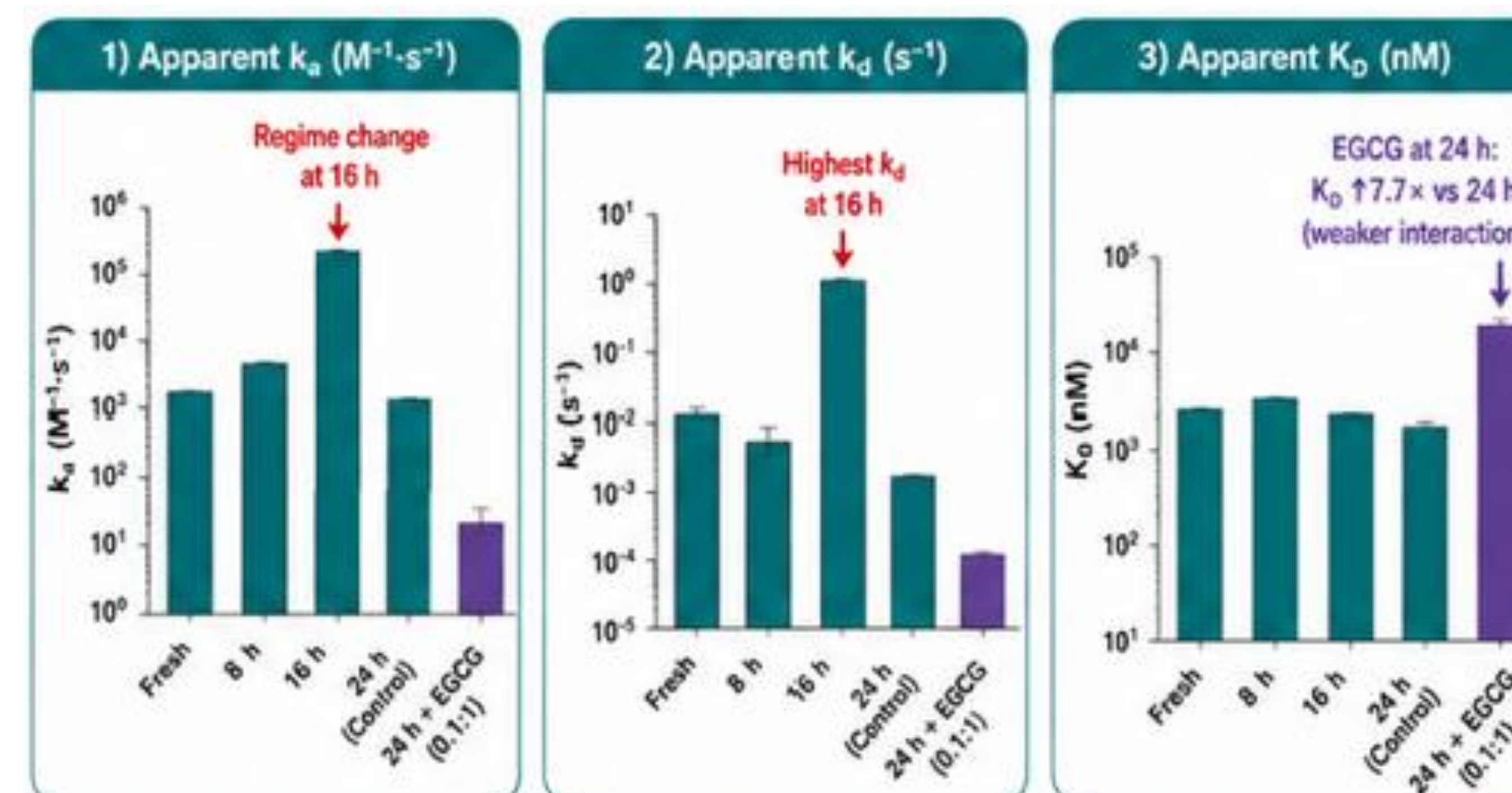
Apparent k_a , k_d , and K_D were derived for comparative profiling

Results

A. Summary of Apparent Kinetic Parameters

Condition	Sample	k_a ($M^{-1}\cdot s^{-1}$)	k_d (s^{-1})	K_D (nM)	Note
Fresh	A β 42	1.25×10^3	2.43×10^{-3}	1.95×10^3	—
8 h	A β 42	4.73×10^3	5.44×10^{-3}	1.15×10^3	—
16 h	A β 42	3.91×10^5	1.08	2.76×10^3	—
24 h	A β 42	1.64×10^3	3.31×10^{-3}	2.02×10^3	Control
24 h + EGCG	A β 42 + EGCG (0.1:1)	3.17×10^1	4.95×10^{-4}	1.56×10^4	$k_a \downarrow 52\times$; $K_D \uparrow 7.7\times$ vs 24 h

B. Kinetic Trends Across Conditions



C. Key Findings

- Incubation time produced pronounced, non-linear kinetic fingerprints
- A β 42 alone showed a dramatic regime change at 16h.
- At 24h, EGCG shifted kinetics toward slower association and weaker effective interaction compared with the 24h control.
- The delayed effect of EGCG suggests modulation of late-stage A β 42 assembly processes.

Conclusions

- A β 42 exhibits time-evolving assembly states with distinct kinetic signatures.
- This is physiologically relevant because oligomeric intermediates are linked to synaptic dysfunction and neurotoxicity, and state-specific kinetics may inform intervention timing.
- FOPPR provides a label-free, real-time kinetic analysis that enables state-resolved profiling of A β 42 assembly-state transitions and inhibitor-dependent kinetic shifts.
- This capability is difficult to obtain from conventional endpoint-only aggregation assays.
- Practical applications include: Low-volume candidate triage, QC of A β preparation state prior to downstream assays, Extension to other amyloidogenic targets.
- Future work will benchmark kinetic fingerprints against orthogonal structural and functional assays.