

Supporting information for

LED-based interferometric reflectance imaging sensor for the detection of amyloid-beta aggregation

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Optical Setup:

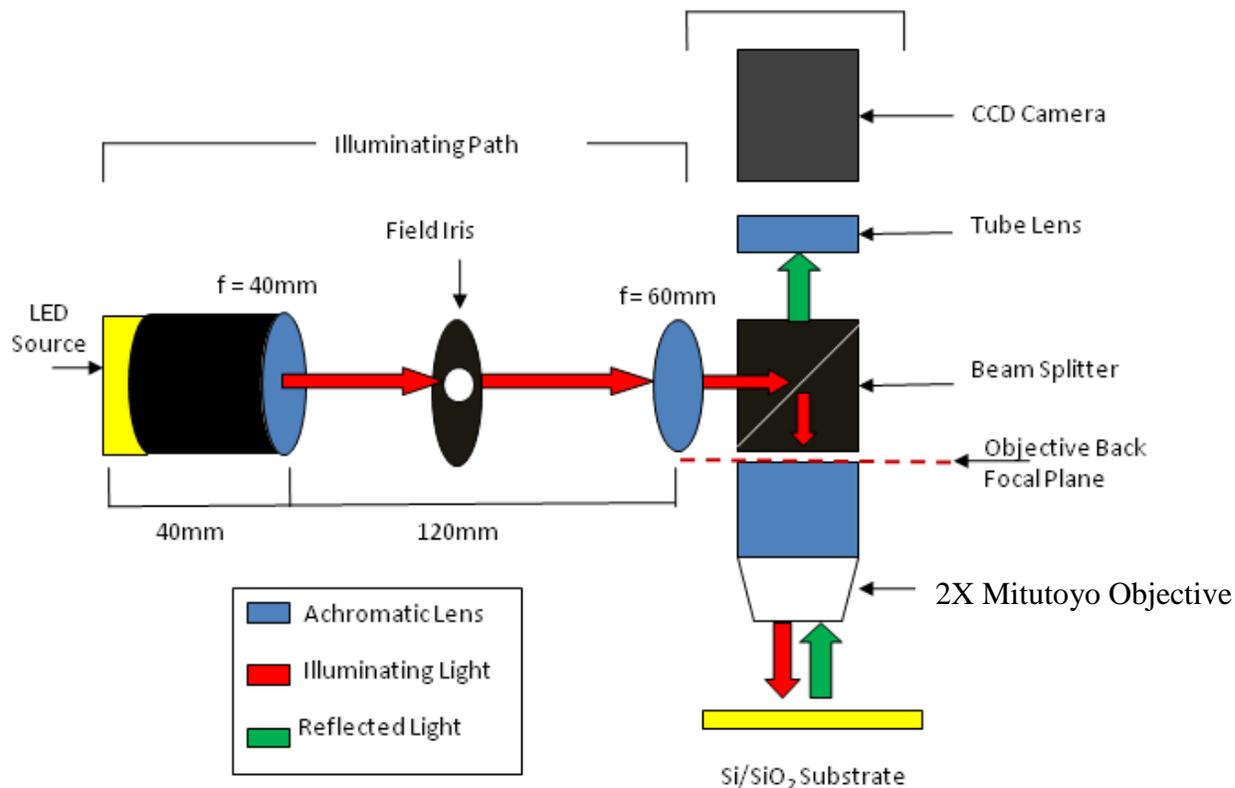


Fig. S-1 Schematic illustration of optical setup. The focal lengths of all lenses are given. Achromatic lenses are shown in blue; IRIS, the beam splitter, and the CCD (Retiga200R, Qimaging) are shown in black. ACULED VHL surface-mount LED package (Perkin-Elmer), which has four independently driven LEDs with peak emission wavelengths of 455 nm, 518 nm, 598 nm, and 635 nm was used.

Data Acquisition and Analysis:

We use the Fresnel reflections to calculate the amount of biomass added on top of the sensor surface by assuming it is an added thickness to the oxide top layer. The wavelength dependence of the Fresnel reflection is used to measure the thickness of the top layer of the sensor which consist of the silicon dioxide and biomass. Referring to equations 1, 2 and 3, shown below, we can determine 'd', the thickness of the top layer when 'R' the reflection coefficient is measured. Equation 1:

$$R = |r|^2 = \frac{r_1^2 + r_2^2 + 2r_1r_2 \cos(2\phi)}{r_1^2 r_2^2 + 2r_1r_2 \cos(2\phi)}$$

where r_1 and r_2 are the Fresnel reflection coefficients of the air-SiO₂ (or buffer-SiO₂) and Si-SiO₂ interfaces respectively. The reflection coefficients can be calculated by Equation 2:

$$r_1 = \frac{n_{ox} - n_1}{n_{ox} + n_1} \text{ and } r_2 = \frac{n_{Si} - n_{ox}}{n_{Si} + n_{ox}}$$

where n_1 , n_{ox} , and n_{Si} are the refractive indices of air (or buffer), SiO₂, and Si respectively. The optical path difference is described by the phase difference, ϕ , from equation 1, which is given

by:

Equation 3:

$$\phi = \frac{2\pi d}{\lambda} n_{ox} \cos\theta$$

Here, d is the thickness of the layer (SiO₂ or SiO₂ + biomass), n_{ox} is the refractive index of SiO₂, λ is the wavelength of the incident light, and the θ is the angle of incidence. IRIS uses low angles of illumination and collection; therefore, the angle of incidence can be assumed to be near zero ($\cos\theta = 1$).

R are measured using the intensity measurements made by the CCD camera when illuminated with the 4 different LEDs sequentially. These data points, (R, λ), are used to fit curves based on Equation 1 for each pixel. Spectral shifts in these Fresnel curves from pixel to pixel are used to determine the corresponding changes in surface thickness.

To monitor changes in biomass on the surface like fibril formation/growth the optical path difference at a region of interest in compared to the background where we expect no change. Fig. S-1 shows how circular spots are analyzed.

All the spots in the field of view (6 mm by 4.5 mm) can be detected/monitored. In the current study, we assumed all fibril growth are only occurring in the seed spots. The software used in this experiment was used to detect circular spots and the detection parameters can be adjusted based on the size of seeds spotted. The average measured height on the spot is subtracted from the average height over an annulus region that is sufficiently far away from the spot such that

even if some fibrils formed out of the central spot, they will not affect the spot height measured. Dust and large contaminants (micron sized objects) will also not fit the Fresnel model; they are rejected because the residual to the fitting surpass a set threshold.

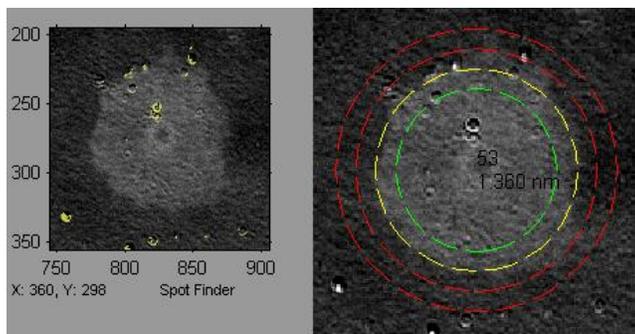


Fig. S-2. Absolute height of each spot was calculated by subtracting the average spot intensity of the background (red region) from that of the spot (green region). Dust particles were detected automatically by the developed MATLAB software as shown in yellow spots, and disregarded in the height calculation.

Scanning Electron Microscopy

In order to monitor the elongated fibril morphology, A β samples incubated in the presence and absence of EGCG or Zn(II) were imaged. As shown in Fig. S-2, it was observed that the Zn(II)-containing seeds showed denser fibril networks compared to those found on A β alone. EGCG-containing seeds displayed amorphous aggregates of dispersed networks, which did not seem to contain mature fibrils. These images supported the LED-IRIS results, which showed EGCG inhibiting the fibril formation on seed spots, while the presence of Zn(II) facilitated its aggregation.

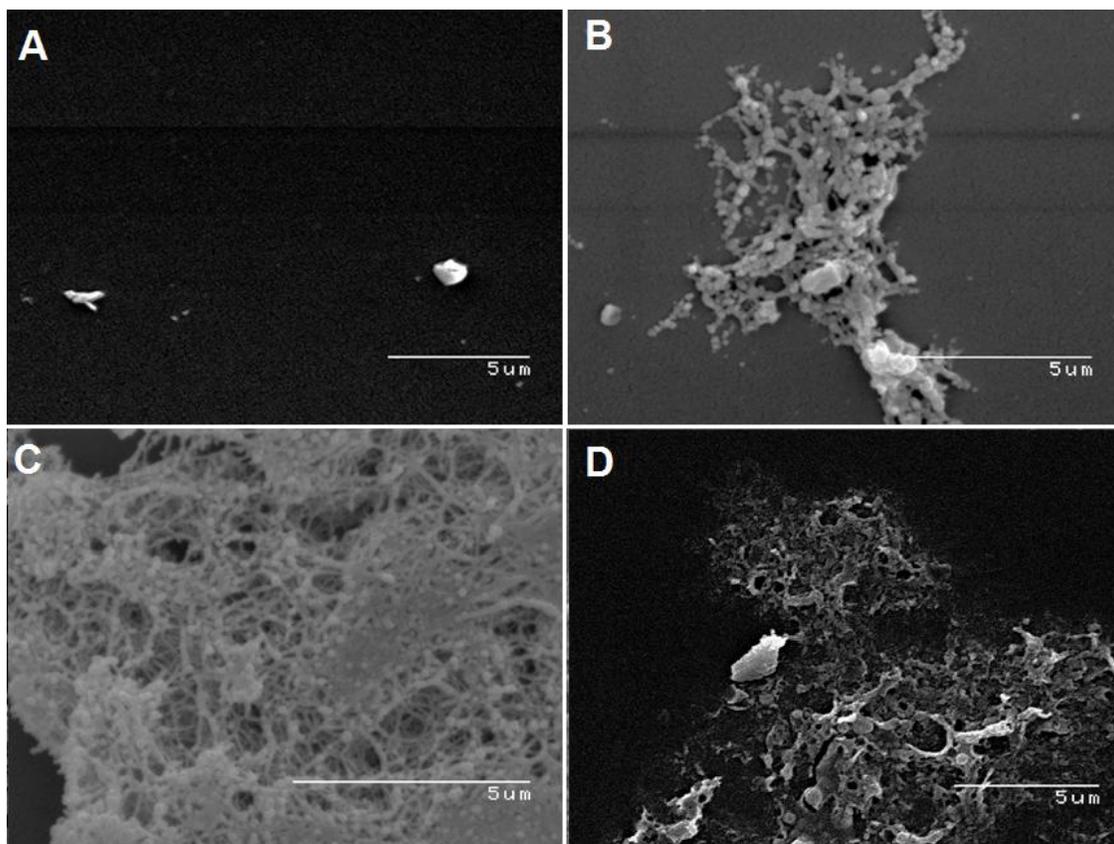


Fig. S-3. Representative SEM images of A β , at the surface of A) an unmodified LED-IRIS chip surface, and modified with B) A β alone, C) A β with Zn(II), and D) A β with EGCG. Other conditions were as described in the Experimental section.

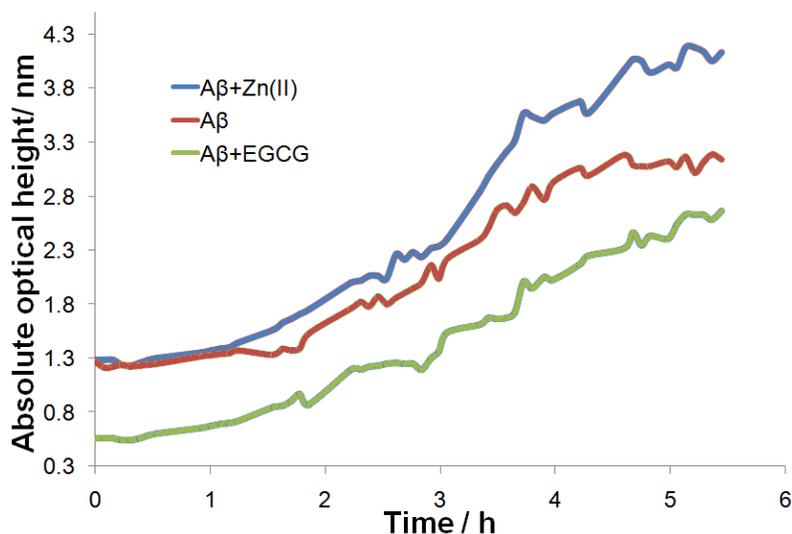


Fig. S-4. Real-time monitoring of signal intensity for high (1:2) amyloid:modulator relative concentrations with monomers flowing at 100 $\mu\text{L}/\text{min}$ through the microfluidic channel. The concentration of A β alone was 200 μM . Other conditions were as described in the Experimental section.

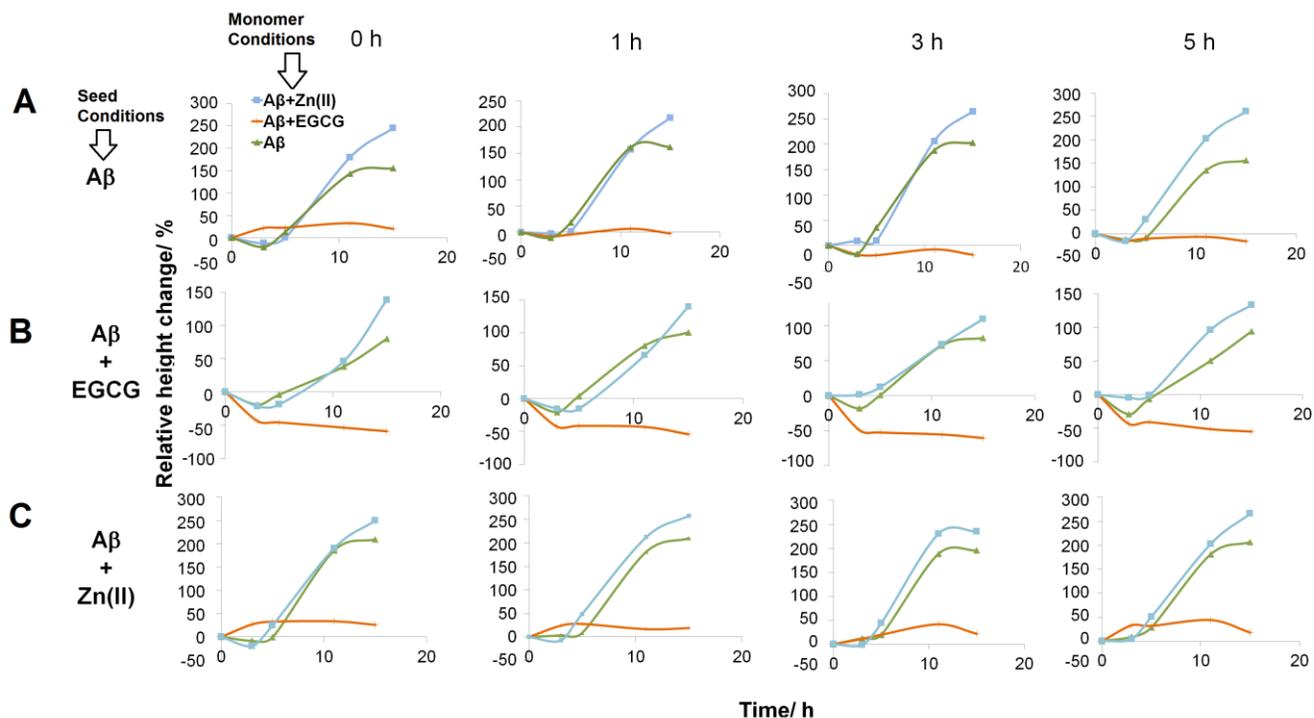


Fig. S-5. Compilation of cross-seeding experimental data using different seed conditions including A) 50 μM A β alone, and A β in the presence of 100 μM B) EGCG and C) Zn(II). Other conditions were as described in the Experimental section.