Determination of the nano-scale adsorption orientation of Peptide

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Background

The geometric analysis and simulation was conducted by assuming a prolate shape of all amyloidogenic peptides. The simulation concluded that a spiking-out orientation of a prolate was required in order to reproduce the extracted peptide coverage ratio, Q. The involvement of a secondary layer was suggested; this secondary layer was considered to be due to the networking of the peptides. Both Ab1-40 and b2m are considered to have a partial charge (especially d+) distribution centering around the prolate axis. The a-syn, on the other hand, possesses a distorted charge distribution. For relatively lower Q (i.e., Q < 0.56), a prolate was assumed to conduct a gyration motion, maintaining the spiking-out orientation in order to fill in the unoccupied space with a tilting angle of approximately 25˚.

Calculation Hypothesis:

#1 Peptide Prolate

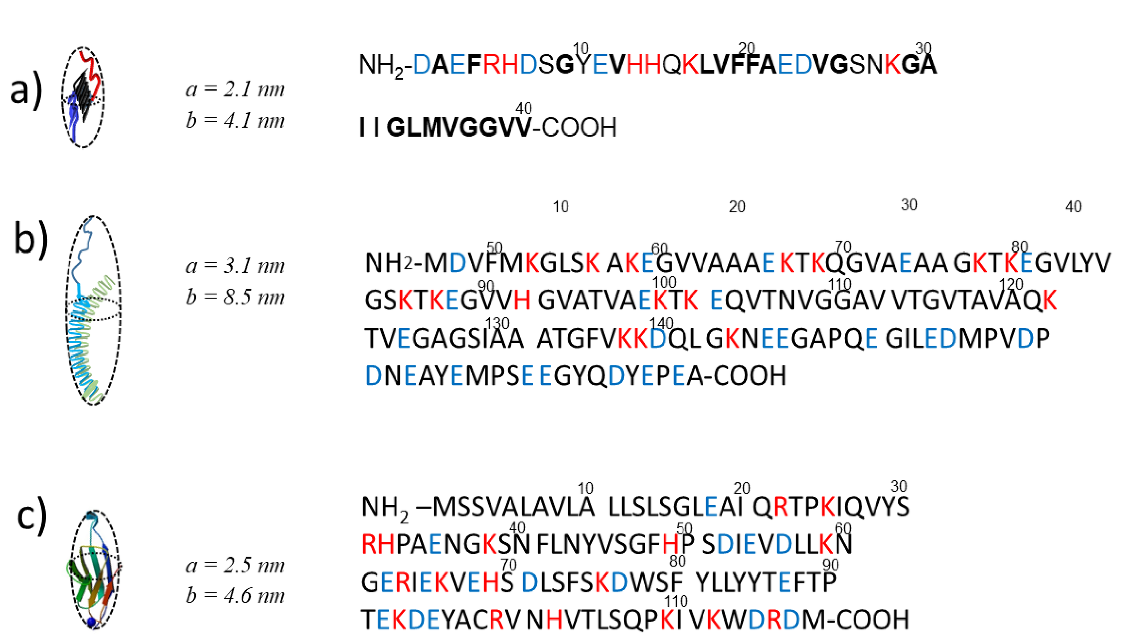
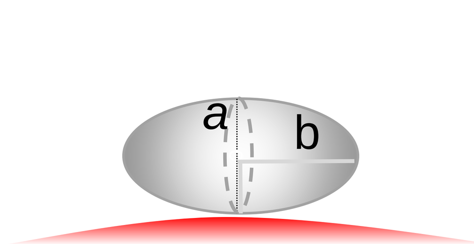
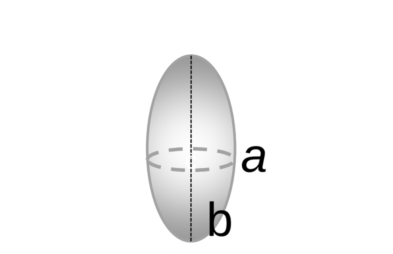


Figure 1. A schematic diagram of sequences for three amyloidogenic peptides a) $A\beta_{1\text{-}40}$, b) α--syn, and c) β2m were assumed to have a prolate shape.

#2 Orientation



We focus on the orientation of the peptide by assuming the peptide shape as a simple prolate. The orientation of this prolate can be roughly considered to be two ways either lay down or spiking out over the spherical surface of nano-gold colloid surface.

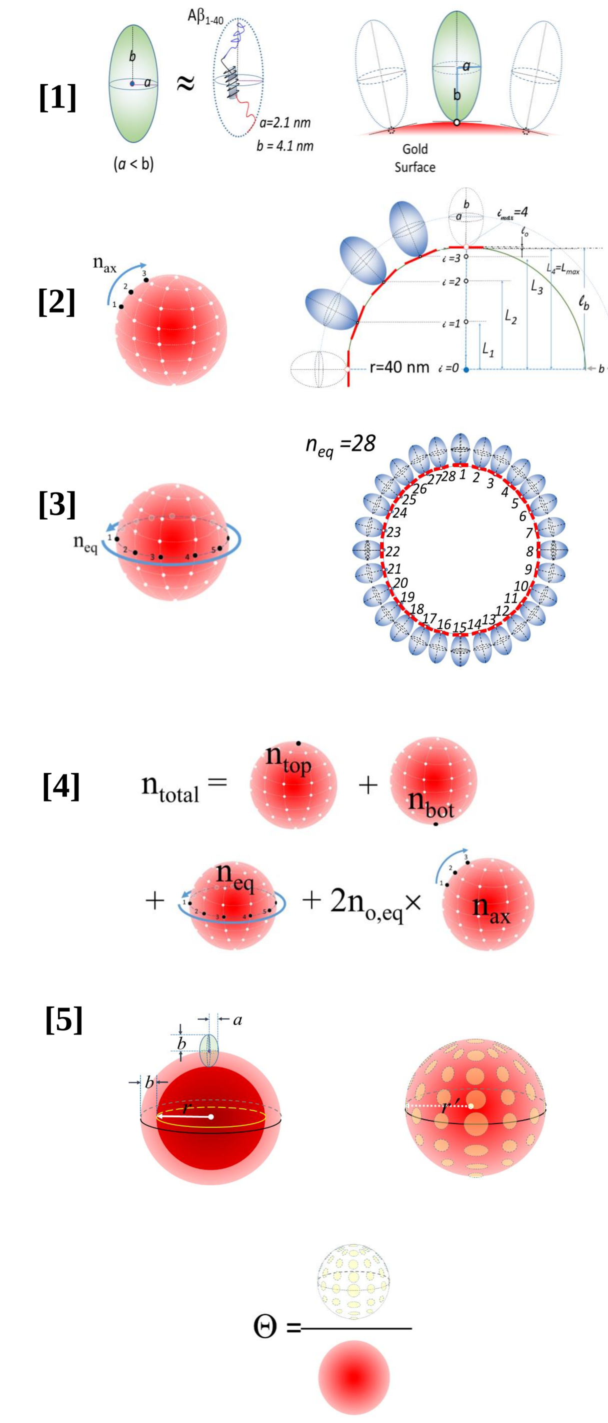


As the first approximation, the lay-down orientation can be more stable and can possess higher interaction between a peptide and gold colloidal surface.

Figure 2. The horizontal and vertical orientation of the prolate were calculated.

Calculation for First Layer:

Figure 3. A schematic procedure simulating the coverage ratio of a peptide over a gold-nano colloidal sphere.



[1] A conceptual sketch indicating that $A\beta_{1\text{-}40}$ was simplified as a prolate top and the expected orientation of a prolate to cover the gold colloidal surface.

[2] A procedure of counting the adsorption point along axial axis; n_{ax}. The detailed procedure of extracting the n_{ax} for the case of gold colloid of d = 30 nm (*d* =30.7 nm).

$$l_b=\sqrt{r^2-b^2} \qquad i_{max}=\left[\frac{a+l_b}{2a}\right]$$

$$n_i=\left[\frac{2\pi+(r_i+a)}{2b}\right],\ r_i=\sqrt{r^2-L_i^2},\ L_i=\frac{l_b-a}{i_{max}}\times i. \qquad n_{eq}=\left[\frac{2\pi+(r+a)}{2b}\right]$$

[3] A procedure of counting the adsorption point along equatorial axis; n_{eq}. The detailed procedure of extracting the n_{eq} for the case of gold colloid of d = 30 nm (*d* =30.7 nm).

$$n_i=\left[\frac{2\pi+(r_i+a)}{2b}\right] \qquad r_i=\sqrt{r^2-L_i^2},\ L_i=\frac{l_b-a}{i_{max}}\times i$$

[4] A procedure of counting total number of adsorption points (n_{total}).

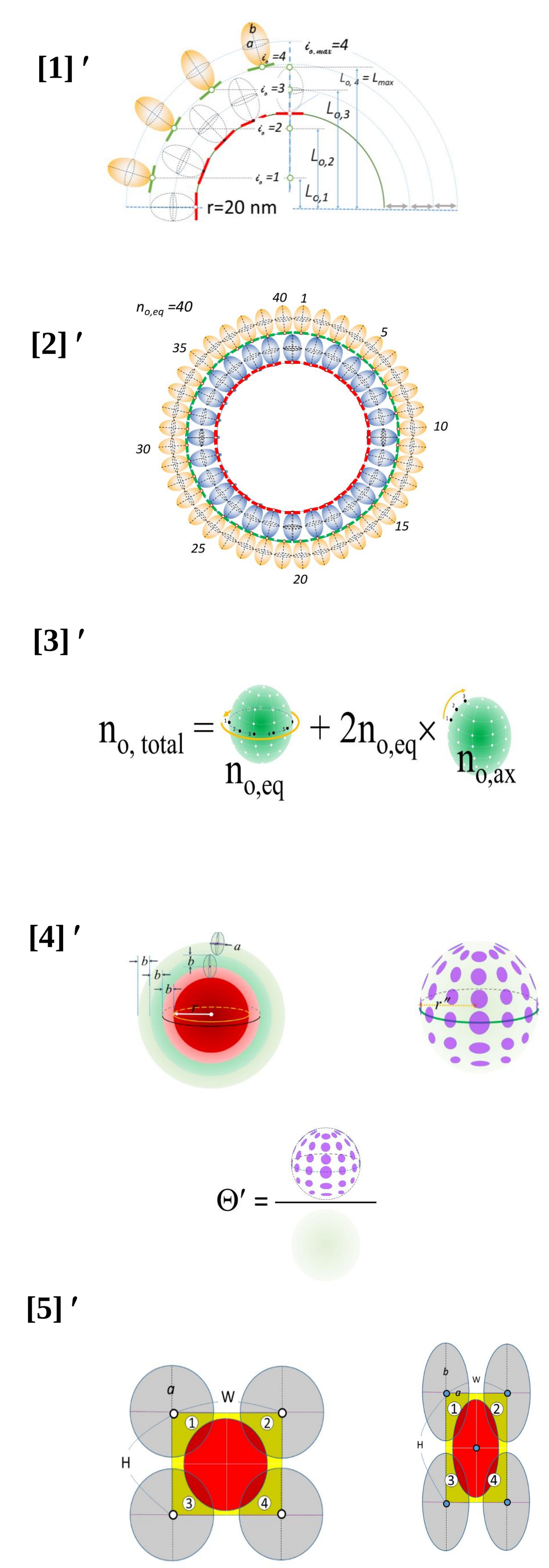
$$\Theta=\frac{A_{prolate}}{A_{sphere}}\times n_{tot}$$

$$A_{prolate}=\pi ab \qquad A_{sphere}=4\pi(r+a)^2$$

[5] A schematic sketch of the imaginary surface area covering the prolate over the nano gold colloid with a radius, r. The concept used to calculate the coverage fraction, (Θ).

Calculation for Second Layer

Figure 4. A schematic procedure simulating the 2nd layer coverage ratio of a peptide over a nano-gold colloidal sphere. Zz



[1]′ A procedure of counting the adsorption point along axial axis; $n_{o,ax}$, over the 2nd layer. The detailed procedure of extracting the $n_{o,ax}$ for the case of gold colloid of d = 30 nm (*d* =30.7 nm)

[2]′ A procedure of counting the adsorption point along equatorial axis; $n_{o,eq}$ over the 2nd layer. The detailed procedure of extracting the $n_{o,eq}$ for the case of gold colloids with a d = 30 nm (*d* =30.7 nm) .

[3]′ A procedure of counting the total number of adsorption points at the 2nd layer ($n_{o,total}$).

[4]′ A schematic sketch of imaginary surface area covering the prolate over the nano-gold colloid with a radius, r. The concept of calculating the coverage fraction, Θ′. When the total coverage ratio for the 1st and 2nd layer was calculated, the overlapped area between both layers was counted once.

$$\Theta'=\frac{A'\times n'_{total}}{A_{sphere}} \qquad \Theta_{Total}=\Theta_{total\,(1st)}+\gamma\,\Theta'_{total\,(2nd)}$$

[5]′ An overall schematic sketch of either optimizing *a* and *b* length of unit prolate in a single layer model for each gold size, as well as the empirical parameter. The combination optimizing *a* and *b* length, were utilized to reproduce the obtained Θ for all gold colloidal sizes under all three amyloidogenic peptides coated over their surfaces.

Results

Table 1. The summary of calculated axial length of prolate (*a* and *b*) for a) $A\beta_{1\text{-}40}$, b) α-syn, and c) β2m. The extracted Θ, Θ_{obs}, was reproduced as Θ_{total} by combining Θ calculated for the 1st layer ($\Theta_{1,cal}$) and for the 2nd layer ($\Theta_{2,cal}$) with the ratio of 2nd Θ cal (γ ($\Theta_{2,cal}$)) used to reproduce the extracted Θ, Θ_{obs}. The number of attached prolates over the 1st layer was shown under n_1.

a) $A\beta_{1\text{-}40}$

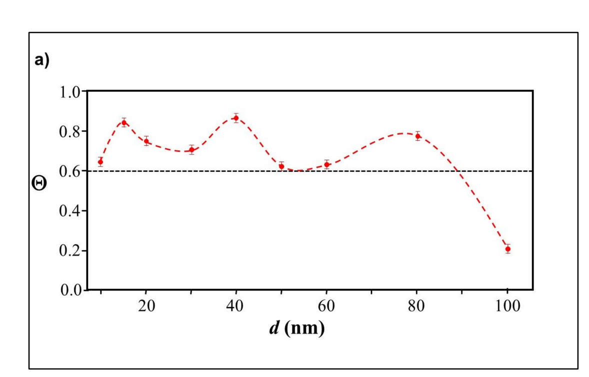
Gold, d (nm)	Gold, d (nm)	a (nm)	b (nm)	n_1	$\Theta_{1,calc}$	$\Theta_{2,cal}$	γ ($\Theta_{2,cal}$)	Θ_{total}	Θ_{obs}
10	9.8 (10)	1.4	2.2	39	0.3791	0.5881	0.4425	0.6393	0.6393
15	15.2 (15)	1.4	2.2	91	0.4643	0.6530	0.5687	0.8357	0.8357
20	19.7 (11)	1.4	2.2	111	0.3746	0.7228	0.5116	0.7443	0.7443
30	30.7(13)	1.4	2.2	287	0.4566	0.7911	0.3027	0.6961	0.6961
40	40.6(11)	1.4	2.2	528	0.5111	0.8449	0.4112	0.8585	0.8585
50	51.5(40)	1.4	2.2	854	0.5357	0.8697	0.0877	0.6119	0.6119
60	60.0(10)	1.4	2.2	1212	0.5728	0.8461	0.0570	0.6210	0.6210
80	80.0(10)	1.4	2.2	2038	0.5608	0.8957	0.2321	0.7687	0.7687
100	99.5(13)	0.905	3.72	597	0.1958	0.1847	0.0023	0.1962	0.1962

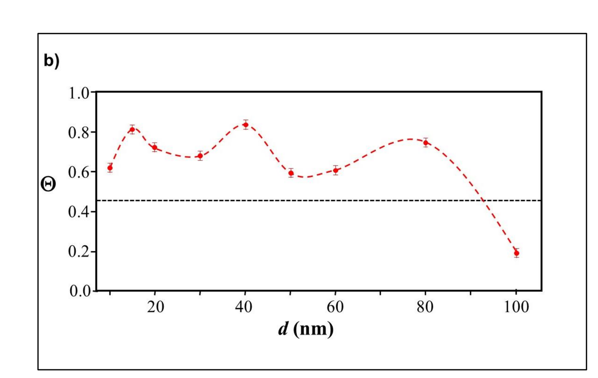
b) α-syn

Gold, d (nm)	Gold, d (nm)	a (nm)	b (nm)	n_1	$\Theta_{1,calc}$	$\Theta_{2,cal}$	γ ($\Theta_{2,cal}$)	Θ_{total}	Θ_{obs}
10	9.8 (10)	4.6	7.4	10	0.3497	0.5099	0.5292	0.6195	0.6195
15	15.2 (15)	4.6	7.4	12	0.2821	0.4600	1.1470	0.8098	0.8098
20	19.7 (11)	4.6	7.4	13	0.2311	0.6876	0.7128	0.7213	0.7213
30	30.7(13)	4.6	7.4	39	0.3986	0.6096	0.4525	0.6745	0.6745
40	40.6(11)	4.6	7.4	48	0.3309	0.7303	0.6860	0.8319	0.8319
50	51.5(40)	4.6	7.4	92	0.4429	0.6588	0.2278	0.5929	0.5929
60	60.0(10)	4.6	7.4	105	0.3971	0.7714	0.2653	0.6018	0.6018
80	80.0(10)	4.6	7.4	186	0.4379	0.7919	0.3876	0.7448	0.7448
100	99.5(13)	1.4	7.4	190	0.1881	0.2056	0.0100	0.1902	0.1902

c) β2m

Gold, d (nm)	Gold, d (nm)	a (nm)	b (nm)	n_1	$\Theta_{1,calc}$	$\Theta_{2,cal}$	γ ($\Theta_{2,cal}$)	Θ_{total}	Θ_{obs}
10	9.8 (10)	2.5	4.6	10	0.4710	0.2414	0.0026	0.4716	0.4716
15	15.2 (15)	2.5	4.6	17	0.1785	0.6403	0.8987	0.7540	0.7540
20	19.7 (11)	2.71	6.41	16	0.4405	0.2687	0.0017	0.4409	0.4409
30	30.7(13)	2.5	4.6	101	0.3965	0.8526	0.4600	0.7887	0.7887
40	40.6(11)	2.5	4.6	175	0.4410	0.8851	0.3460	0.7473	0.7473
50	51.5(40)	2.5	4.6	276	0.4682	0.9061	0.3081	0.7473	0.7473
60	60.0(10)	2.98	4.25	88	0.4709	0.4832	0.0055	0.4735	0.4735
80	80.0(10)	2.5	4.6	666	0.5231	0.9843	0.3676	0.8850	0.8850
100	99.5(13)	2.98	4.25	1025	0.5479	0.99973	0.4424	0.9902	0.9902





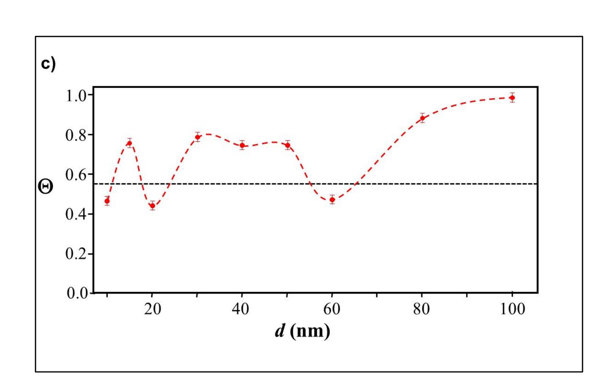


Figure 5. A plot for experimentally obtained Θ for a) $A\beta_{1\text{-}40}$, b) α-synuclein, and c) β2m. A blue solid line composed of a collection of simulated values described in the text. The dotted line shows an upper limit of the Θ value obtained by a single layer model.

References

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Discussion

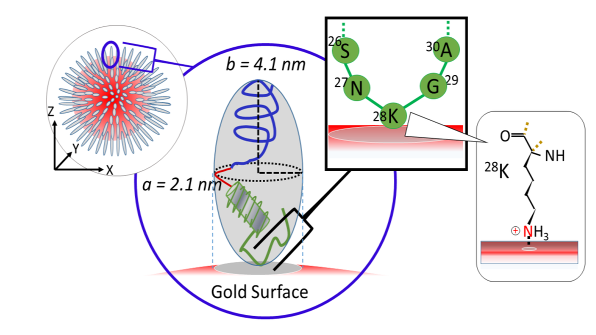

Figure 6. The proposed attachment structure of $A\beta_{1\text{-}40}$ over the surface of a gold colloidal particle.

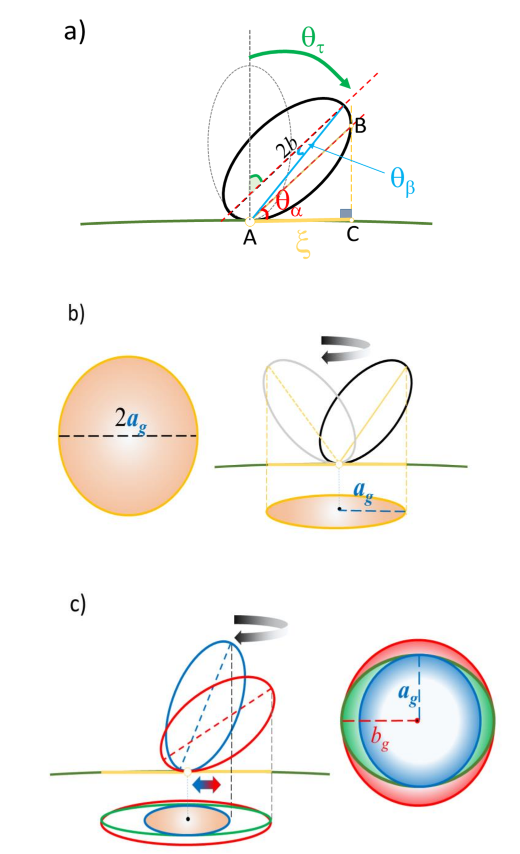

Figure 7. A sketch of the side view of a rotating prolate. a) The tilting of a prolate over the nano-gold surface and approximation for radius (L) of the circular plane over the nano surface. b) A rotational motion of a prolate with a fixed contacting point, resulting in a circular occupied space over the surface. c) A gyration motion of a prolate with a movable contacting point, resulting in an oval occupied space over the surface.

Table 2. The list of extracted tilting angles (θ_α and θ_β) for the lower coverage for a) $A\beta_{1\text{-}40}$, b) α-syn, and c) β2M.

a) $A\beta_{1\text{-}40}$	
d	99.5
b	2.200
a_g	3.720
θ_τ	57.721º
θ_α	32.279º
θ_β	0.155º
b_g	0.905
θ_τ	11.870º
θ_α	78.130º
θ_β	0.565º

b) α-syn	
d	99.5
b	7.400
a_g	7.400
θ_τ	30.000º
θ_α	60.000º
θ_β	0.000º
b_g	1.40
θ_τ	5.428º
θ_α	81.247º
θ_β	0.127º

c) β2m			
d	9.80	19.7	60.0
b	4.6	4.6	4.6
a_g	4.03	6.41	5.40
θ_τ	25.980º	44.166º	35.942º
θ_α	64.020º	45.834º	54.058º
θ_β	0.354º	0.064º	0.326º
b_g	2.70	2.73	4.80
θ_τ	17.067º	17.262º	31.449º
θ_α	72.933º	72.738º	58.551º
θ_β	0.508º	0.234º	0.060º

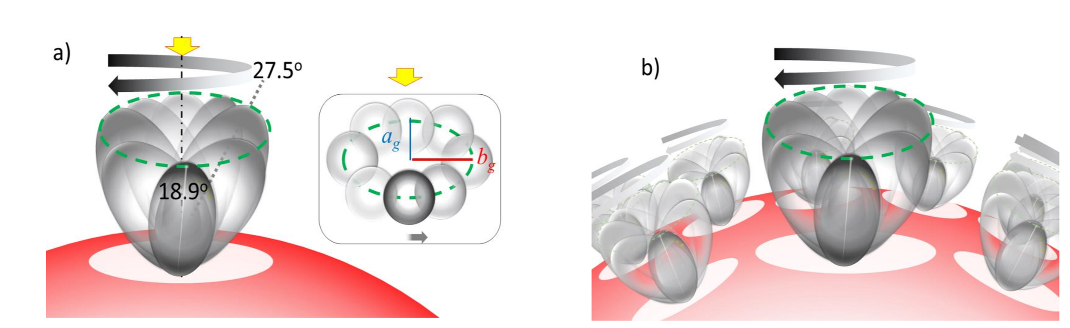

Figure 8. a) The sketch showing the gyration motion of a prolate (*a* = 2.5 nm and *b* =4.6 nm) representing β2m over a gold nano-particle with a diameter of d = 60 nm, where the prolate major axis tilts between 27.5° and 18.9° as it rotates over the surface. It results in an oval occupied space with *a* = 2.98 nm and *b* = 4.25 nm. (See Table 3) b) The sketch of a gyrating prolate over the nano-gold particle surface.

Conclusions

The surface properties of nano-gold colloidal surfaces due to adsorption of amyloidogenic peptides were successfully monitored and characterized by observing the response of spectroscopic features as a function of an external pH change. This surface property change was found to be linearly correlated with the coverage ratio of the peptide, Θ. With the simplification of the space occupied by a peptide into a prolate, the Θ was extracted through a simplified tessellation logic applied for a sphere. The simulation suggested that a prolate needs to have a spiking-out orientation with prolate axial length of (*a*, *b*) = (1.4 nm, 2.2 nm) for $A\beta_{1\text{-}40}$, (*a*, *b*) = (4.6 nm, 7.4 nm) for α-syn, and (*a*, *b*) = (2.5 nm, 4.6 nm) for β2m. The segment possesses a δ+ that was considered to be highly used when $A\beta_{1\text{-}40}$ and β2m each interacted with nano-gold colloidal surface. This possesses a distribution of centering around the prolate axis. On the other hand, the δ+ of α-syn was used to interact between each monomer, and the charge distribution was spread around with a distortion, resulting in a high exposure for the counter acting monomer.