On a Potential Sodium Effect in Fibrillar Amyloid-β Oligomers

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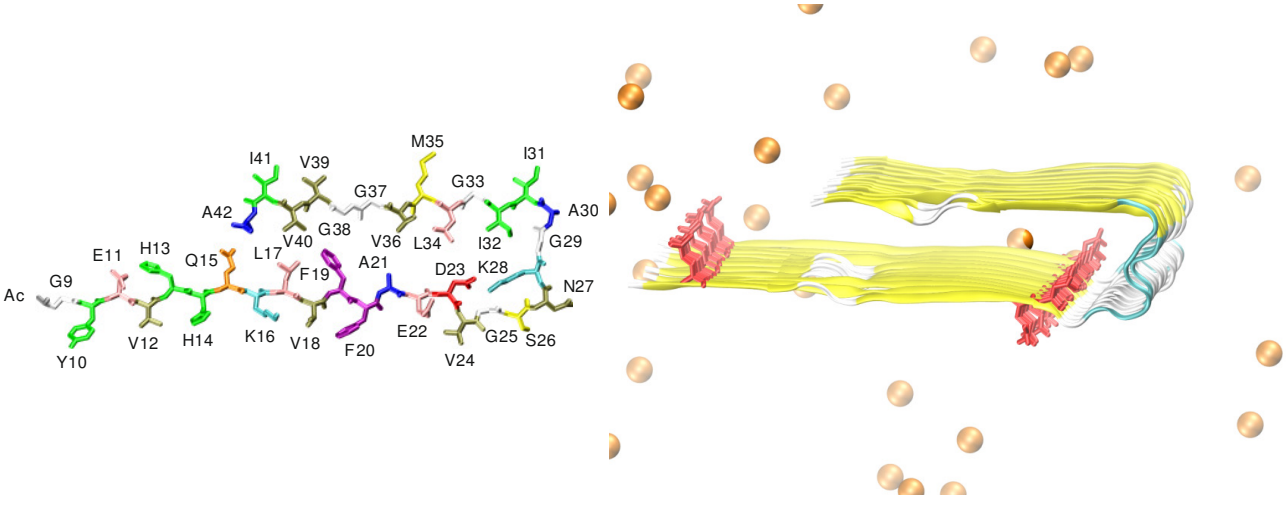
The aggregation of amyloid-β (Aβ) peptide into oligomers and fibrils is the hallmark in Alzheimer's Disease (AD). Nowadays, small soluble oligomers are believed to be the most neurotoxic species, probably the causative agents in AD. Aβ fibrils on the other hand may serve as reservoirs for small toxic oligomers. While it is well known from experiment, that the aggregation process is modulated by salt concentration in solution, the molecular details of the underlying interactions are not.

Salts occur ubiquitously in physiological environments and are known to have profound effects on the solubility of proteins (Hofmeister series). Monovalent alkali metal ions exhibit a more subtle effect on Aβ aggregation in experiment than doubly charged species [1,2].

In this contribution we investigate the so-called 'sodium-effect' on fibrillar Aβ oligomers. This effect modulates the self-organization of amphiphilic carboxylates in forming micelles: Na+ is able to form bridging complexes with carboxylate groups, in contrast to K+ [3].

A systematic series of molecular dynamics simulations of single and double layer fibrillar Aβ oligomers in aqueous 150 mM salt solution provides insights about the stabilizing interactions between the cations and charged Aβ key residues (e.g. Glu22). The current results show similarities and differences with a previous computational study, which lacked a physiological ion concentration in the solvent [4]. Interestingly, metal ions can access the water channel present in fibrillar Aβ species, which is located in the turn region. The ions use the same entry paths found previously for water molecules [4].

Furthermore, Na+ and K+ ions exhibit a different interaction behaviour with the fibrillar Aβ oligomers. This suggests the existence of a sodium effect in this species.



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