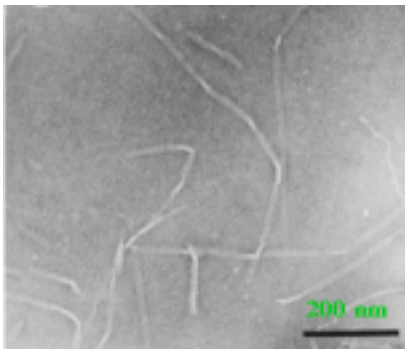


Biophysical studies of amyloids and their interactions with accessory molecules.

A third area of interest in our group, is the mechanisms of amyloid fibril assembly [22]. *In vivo*, amyloid fibril formation is not a simple self-assembly process, but a process that involves a number of cofactors such as glycosaminoglycans (GAGs) and heparan sulfate proteoglycans [38]. This poses the question of what factors are responsible for these interactions, particularly since the polysaccharides are highly polar and negatively charged while the cores of the amyloid fibrils are presumably highly shielded from water.



Long-term goals:

- Binding of GAGs has been investigated for a number of proteins involved in amyloid pathology[38]. To better understand the mechanism of recognition, we are planning to look at the binding of GAGs to CspA, an *E coli* protein that forms aggregates with the characteristics of amyloid at acidic pH [22]. The rationale for these investigations is to see if binding of GAGs is unique to the twenty or so proteins implicated in amyloid disease, or a more general property of proteins that form amyloid.
- We have initiated studies on the interactions of cofactors with amyloids involved in Parkinson's disease and Alzheimer's disease.

Recent Publications:

- 1) Alexandrescu, A.T. (2001) "An NMR-based quenched hydrogen exchange investigation of model amyloid fibrils formed by the protein CspA". *Pac. Symp. Biocomput.* 6, 67-78.
- 2) Alexandrescu, A.T. (2005) "Amyloid Accomplices and Enforcers" *Protein Science* 14, 1-12.

References:

22. Alexandrescu AT, Rathgeb-Szabo K: **An NMR investigation of solution aggregation reactions preceding the misassembly of acid-denatured cold shock protein A into fibrils.** *J Mol Biol* 1999, **291**:1191-1206.
38. Alexandrescu AT: **Amyloid accomplices and enforcers.** *Protein Sci* 2005, **14**:1-12.
39. Alexandrescu AT: **An NMR-based quenched hydrogen exchange investigation of model amyloid fibrils formed by cold shock protein A.** *Pac Symp Biocomput* 2001:67-78.