Supplementary material

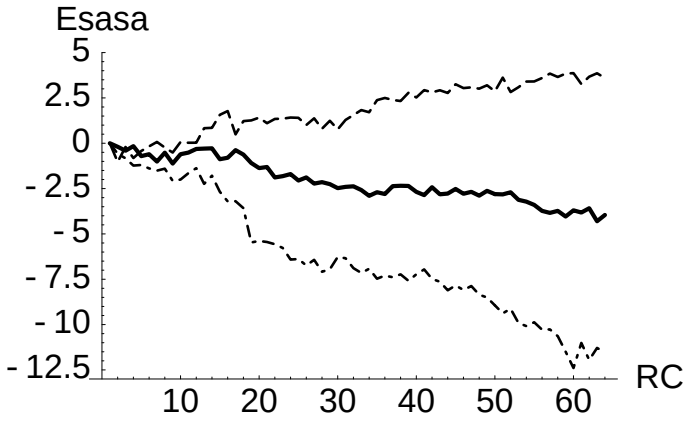

Fig. 12. Solvent Accessible Surface Area contribution to the free energy in kcal/mol. Single strand (broken line), 3 peptide stack (full line) and single strand on top of a plane of 4 fixed β sheets (dash-dotted line). For conversion from surface area to free energy the factor $0.025 \frac{kcal}{mol \cdot A^2}$ *was employed.*

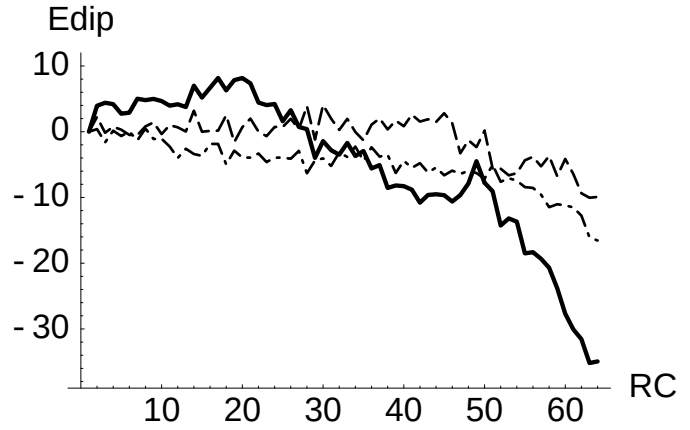

Fig. 13. Electrostatic energies due to peptide backbone dipoles as a function of $\alpha \rightarrow \beta$ *reaction coordinate in kcal/mol. Single peptide strand (broken line), 3 stack (full line) and single strand on top of a plane of 4 fixed β sheets (dash-dotted line).*

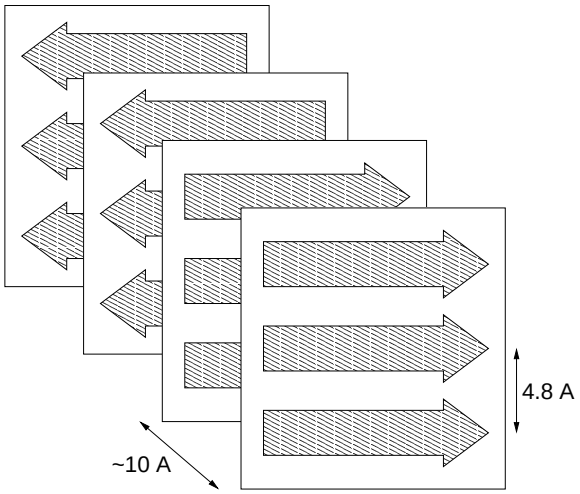

Fig. 14. Proposed packing of GNNQQNY in the microcrystals, a total of 12 strands is shown.

Model building

In order to create atomic resolution models to fit the x-ray powder patterns of the Eisenberg lab (ref), we first locate 3 candidate peptide structures in the pdb all of which have 4 residues the same as GNNQQNY. These are 2bpa (GRVQQTY), 1agd (GHNQYAY) and 1jlx (GHYTQNY). Using the built-in mutation function of SwissPDB Viewer we use these to generate 3 initial conformations.

The X-ray pattern fitting part is then performed with CNS v1.1 using an iterative technique. If two or more sets of indices (hkl's) correspond to a single peak in the powder pattern, it is assumed that they make the same contribution to the intensity in an initial fit. Based on the so-obtained F_{obs}'s, a round of cross-rotational and translational search was run under CNS. After the search is done, F_{calc}'s are evaluated from the best model (the one with the lowest R-value). This ends the first round of iteration. In the second round, a second set of F_{obs}'s is evaluated, this time for overlapping indices. It is assumed that the contributions they make to the peak intensity are proportional to the squares of the first round Fcalc's. The remaining steps are as before. Such an iteration round is repeated five times. The model is further refined by annealing methods. The initial temperature is set to 5000 degrees. After each round of annealing the F_{calc}'s are reevaluated from the model, and the F_{obs}'s for the next round are updated according to those F_{calc}'s. This iteration step is first repeated five times making use of the lower half of the powder peaks only since they are more important than the higher half, and then repeated five times again, this time taking advantage of the whole data set.

A final step is a real space search. We take the first atom in the PDB file, and test respectively if a trial displacement $\pm$ 0.1 Å in its x, y, or z coordinate will cause a decrease in the R-value, then pick among these trial positions the one that gives the lowest R-value. The same process is repeated successively for the other atoms. After each atom has been treated once in such a way, we apply energy minimization (using the built-in function of SwissPDB Viewer) to remove possible chemical violations and fix the bond lengths. This completes a round of real space search, which is again repeated 20 rounds.

The results of the fitting are shown in figure 14, where the calculated line (black) is that after fitting the peptide taken from the file 2bpa. It should be emphasized that the fitting to the low-s peaks, plays the most important role in the model building since they are less sensitive to perturbations of the atom positions and generally correspond to rather few sets of indices (hkl's).

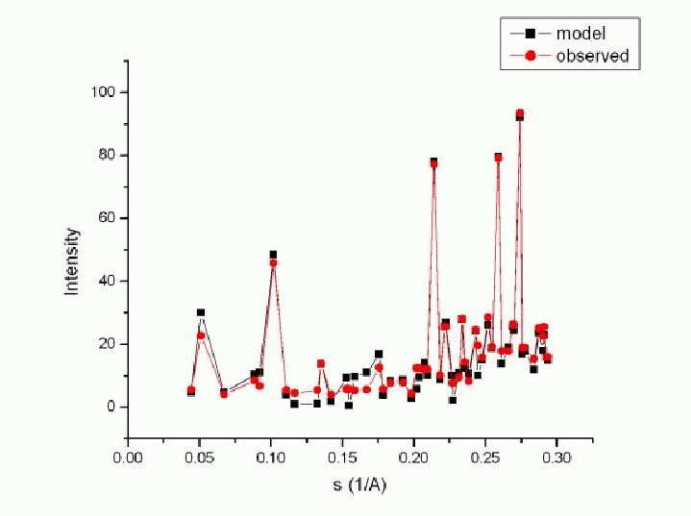

Fig. 15. Fitting (red) to the diffraction data obtained from GNNQQNY microsrystals (black) by Eisenberg and coworkers [1]

References

[1] M. Balbirnie, R. Grothe, D. S. Eisenberg, An amyloid-forming peptide from the yeast prion sup35 reveals a dehydrated β-sheet structure for amyloid, Proc. Natl. Acad. Sci. USA 98 (2001) 2375–2380.