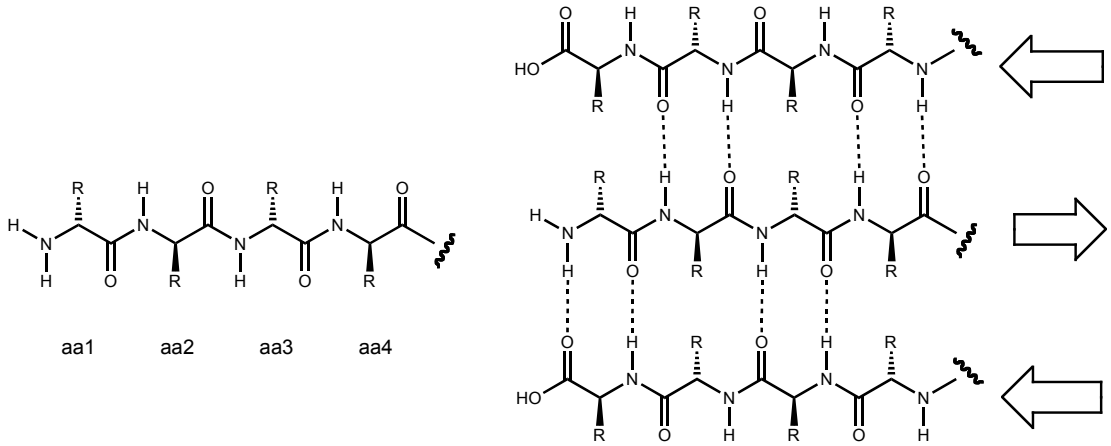
CH3F5 Molecular Interactions Workshop Additional Material

Part 1 Peptides are known to assemble into β-sheet structures (below). Estimate how many amino acids would be needed to achieve an association constant of 10^5 M^{-1} between **two** polypeptides aligned in this fashion in chloroform.

HB donor parameter α amide = 2.9
HB acceptor parameter β amide = 8.3

HB donor parameter α chloroform = 2.2
HB acceptor parameter β chloroform = 0.8



Part 2 If the corresponding HB acceptor value for DMSO, a competitive solvent is: β = 8.9, estimate what percentage of this solvent would you have to add to the above peptide in chloroform required to reduce the association constant 10,000-fold?

Part 1 suggested answer:
$\Delta G = -(\alpha-\alpha_s)(\beta-\beta_s) + 6$ kJ mol^{-1}
For two side-by-side peptide chains, only every OTHER amino acid actually bonds with an ADJACENT peptide. So for *n* amide HBs, there will be 2*n* amino acids required, but this multiplier will be used after calculating *n*.

$\Delta G = -n(2.9-2.2)(8.3-0.8) + 6$ kJ mol^{-1}

Now $\Delta G = -RT\ln K_a$
If R = 0.008314 $kJK^{-1}mol^{-1}$
Hence $-n(2.9-2.2)(8.3-0.8) + 6 = -RT \ln 100\,000$

Rearrange:
$-n(2.9-2.2)(8.3-0.8) = -RT \ln 100\,000 - 6$

$-n(2.9-2.2)(8.3-0.8) = -(RT \ln 100\,000+6)$

$n = (RT \ln 100\,000+6)/(2.9-2.2)(8.3-0.8)$

$n = 34.52/5.25 = 6.6$

Hence n = 7 hydrogen bonds, which equates to 7 amino acids by rounding up since only every *other* amino acid will hydrogen bond to a given adjacent peptide chain (the 7th hydrogen bond is on the 7th amino acid … try drawing the structure!)

Part 2 One way of looking at this problem might be …

$\Delta G = -RT\ln K_a$

Hence $\Delta G = \Delta\Delta G_{HB\ Tot} = -RT \ln 10$ if the K_a reduced from 100 000 to 10 M^{-1}.

Where $\Delta\Delta G_{HB\ Tot} = (1-x)\Delta\Delta G_{HB}\ (CHCl_3) + x\,\Delta\Delta G_{HB}\ (DMSO) + 6$ kJ mol^{-1}

Now for the above 7 amino acids (which actually form 6 or 8 hydrogen bonds with an adjacent chain, depending on which you consider):

in $CHCl_3$, $\Delta\Delta G_{HB}\ (CHCl_3) = -8(2.9-2.2)(8.3-0.8)$ kJ mol^{-1}

And for 8 HB in DMSO, $\Delta\Delta G_{HB}\ (DMSO) = -8(2.9-0.8)(8.3-8.9)$ kJ mol^{-1}

Hence $-(8(2.9-2.2)(8.3-0.8)\ (1-x) - 8((2.9-0.8)(8.3-8.9)\ x + 6 = -0.008314 \times 298 \times \ln 10$

$-42(1-x) + 10.08\,x + 6 = -0.008314 \times 298 \ln 10$

$42x + 10.08\,x - 36 = -0.008314 \times 298 \ln 10$

$52.08\,x = -0.008314 \times 298 \ln 10 + 36$

$= 30.295/52.08$

$x = 0.58$

x = **58 mol% of DMSO** required to reduce the association constant from 100 000 to 10 for two 7-mer peptides associated as β-sheet.