The Energy Landscapes Framework

David J. Wales

University Chemical Laboratories, University of Cambridge,
Lensfield Road, Cambridge CB2 1EW, U.K.

The potential energy landscape provides both conceptual and computational tools for understanding a wide range of observable properties in molecular science.[1–4] In particular, we can exploit stationary points (minima and transition states) for structure prediction and analysis of global thermodynamic and kinetic properties. Basin-hopping global optimisation[5] represents a powerful tool for structure prediction, while basin-sampling/parallel tempering[6,7] and discrete path sampling[8–10] enable us to address broken ergodicity and rare event dynamics. Basin-hopping and basin-sampling require only local minimisation; discrete path sampling involves location of transition states between local minima. This coarse-graining in terms of stationary points is founded upon efficient geometry optimisation procedures; the corresponding software and energy landscape databases are available at URL http://www-wales.ch.cam.ac.uk.

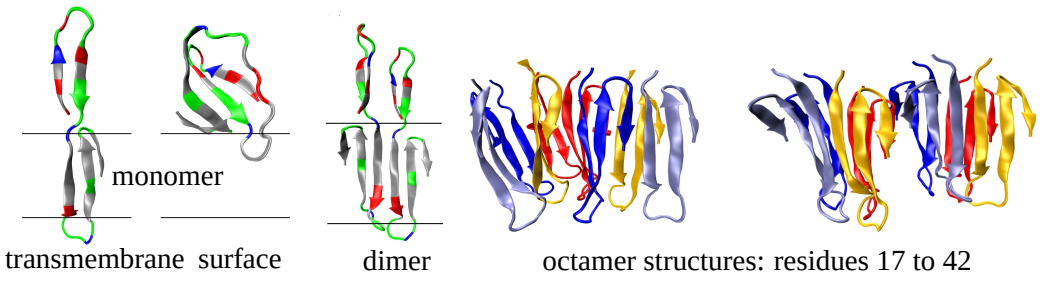
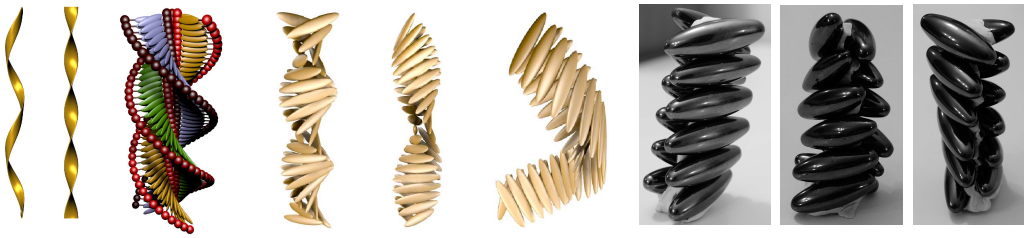


Figure 1: Predicted structures for Aβ_{1-42} monomer (transmembrane and surface structures, left), dimer (middle) and octamer (right) in contact with an implicit membrane.

Applications have been presented ranging from prediction and interpretation of high resolution spectra for small water clusters,[11,12] folding and misfolding of biomolecules,[13–15] to the analysis of structural glass-formers[16,17] and condensed soft matter systems.[18,19] Some recent results for small oligomers of the Aβ_{1-42} peptide are illustrated in Figure 1.[20] These structures were obtained using CHARMM19[21] with the implicit membrane potential IMM1.[22] A basin-hopping/parallel tempering scheme with exchanges between basin-hopping runs at different temperatures was used,[20] together with intra- and intermolecular coordinate moves for the peptides. The most favourable monomer transmembrane structure has residues 17 to 42 inserted in the membrane. The most stable octamer structures can be viewed as displaced tetramers composed of two or three β-sheets.[20]



helical fibre morphologies bilayer filaments magnetic bilayers

Figure 2: Left: introduction of a cytochrome domain into an amyloid fibre can change the morphology from twisted to spiral ribbons and induce systematic kinking. Centre: rigid building blocks consisting of two ellipsoids can reproduce these structures. Right: the structure depends mostly on the internal geometry of the building blocks.

Coarse-grained modelling has been used to explain the underlying principles that lead to the emergence of shells, tubes, helices and spirals.[18,19] Recently we have discovered design principles that connect the morphology of amyloid fibres to seedpods and macroscopic helices formed from elliptical magnets (Figure 2).[23] Experimentally, the introduction of a cytochrome domain into an amyloid fibre permits dynamic adjustment of the fibre morphology via heme binding.[24] The interlocking of fibre filaments introduces systematic kinking,[24] and a transition from a twisted ribbon to a spiral ribbon morphology was also observed.[25] By constructing a rigid link between two anisotropic interacting units we have now shown that the precise helical morphology of aggregates formed from such a composite building block primarily depends on the internal geometry, rather than the nature of the interaction or the anisotropy of the interacting units. This framework can be viewed as a discrete version of the bilayered frustration principle, which drives the morphological transitions of the Bauhinia seedpod.

References

[1] D. J. Wales, *Energy Landscapes*, Cambridge University Press, Cambridge (2003).

[2] D. J. Wales, Phil. Trans. Roy. Soc. A **363**, 357 (2005).

[3] D. J. Wales and T. V. Bogdan, J. Phys. Chem. B **110**, 20765 (2006).

[4] D. J. Wales, Curr. Op. Struct. Biol. **20**, 3 (2010).

[5] D. J. Wales and J. P. K. Doye, J. Phys. Chem. A **101**, 5111 (1997).

[6] T. V. Bogdan, D. J. Wales and F. Calvo, J. Chem. Phys. **124**, 044102 (2006).

[7] D. J. Wales, Chemical Physics Letters **584**, 1 (2013).

[8] D. J. Wales, Mol. Phys. **100**, 3285 (2002).

[9] D. J. Wales, Mol. Phys. **102**, 891 (2004).

[10] D. J. Wales, Int. Rev. Phys. Chem. **25**, 237 (2006).

[11] T. R. Walsh and D. J. Wales, J. Chem. Soc. Faraday Trans. **92**, 2505 (1996).

[12] D. J. Wales and T. R. Walsh, J. Chem. Phys. **106**, 7193 (1997).

[13] P. N. Mortenson, D. A. Evans and D. J. Wales, J. Chem. Phys. **117**, 1363 (2002).

[14] D. A. Evans and D. J. Wales, J. Chem. Phys. **119**, 9947 (2003).

[15] B. Strodel, C. S. Whittleston and D. J. Wales, J. Amer. Chem. Soc. **129**, 16005 (2007).

[16] D. J. Wales and J. P. K. Doye, J. Chem. Phys. **119**, 12409 (2003).

[17] V. K. de Souza and D. J. Wales, J. Chem. Phys. **129**, 164507 (2008).

[18] S. N. Fejer and D. J. Wales, Phys. Rev. Lett. **99**, 086106 (2007).

[19] D. Chakrabarti, S. N. Fejer and D. J. Wales, Proc. Nat. Acad. Sci. USA **106**, 20164 (2009).

[20] B. Strodel, J. W. L. Lee, C. S. Whittleston and D. J. Wales, Journal of the American Chemical Society **132**, 13300 (2010).

[21] E. Neria, S. Fischer and M. Karplus, J. Chem. Phys. **105**, 1902 (1996).

[22] T. Lazaridis, Proteins: Struct., Func. and Gen. **52**, 176 (2003).

[23] C. J. Forman, S. N. Fejer, D. Chakrabarti, P. D. Barker and D. J. Wales, The Journal of Physical Chemistry B **117**, 7918 (2013).

[24] C. J. Forman, A. Nickson, S. Anthony-cahill, G. Kaggwa, U. Feber, K. Sheikh, J. Suzanne and P. Barker, ACS Nano **6**, 1332 (2012).

[25] A. J. Baldwin, R. Bader, J. Christodoulou, C. E. MacPhee, C. M. Dobson and P. D. Barker, J. Am. Chem. Soc. **128**, 2162 (Feb. 2006).