Molecular Modelling

The receptor model was created using the automatically generated WHATIF model based upon the bacteriorhodopsin template as a starting point. Modifications to this starting conformation were made using the SYBYL modelling software from TRIPOS to produce a sensible, energetically favourable structure which conformed to our in-house results. These modifications included helix rotations and translations as well as the introduction of the loop regions between each helix including dynamics and energy minimisations (TRIPOS forcefield, Gasteiger-Huckel charges with neutral amino acids) with and without agonists bound.

References for the WHATIF programme:

(1) Horn, F.; Weare, J.; Beukers, M. W.; Horsch, S.; Bairoch, A.; Chen, W.; Edvardsen, O.; Campagne, F.; Vriend, G. GPCRDB: an information system for G-protein coupled receptors. *Nucleic Acids Res.* **1998**, *26 (1)* , 275-279.

(2) Web reference: http://swift.embl-heidelberg.de/7tm/

References for TRIPOS:

(1) TRIPOS Inc. 1699 S. Hanley Road, St. Louis, MO USA.

(2) Web reference: www.tripos.com.