Urotensin-Related Peptide (URP) Long-term Molecular-Dynamics Simulation

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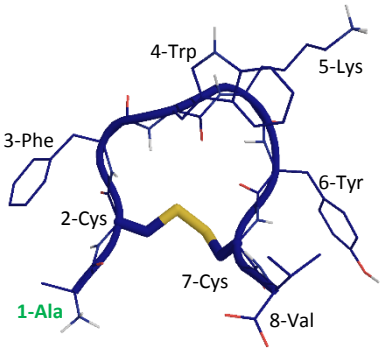

Urotensin-related peptide: Ala-[Cys-Phe-Trp-Lys-Tyr-Cys]-Val
(Human-UII: Glu-Thr-Pro-Asp-[Cys-Phe-Trp-Lys-Tyr-Cys]-Val)

The hormone peptides URP (urotensin-related peptide) and U-II (urotensin II) are the natural ligands of the urotensinergic GPCR (G-protein coupled receptor) system, which plays an important role in the regulation of the cardiovascular system. Besides their physiological function, URP and U-II are also linked to pathophysiological processes such as hypertension [1].
URP is an octapeptide with a six-residue ring closed by a 2Cys-7Cys-disulphide bridge, a 1-Ala N-terminal and an 8-Val C-terminal. URP differs from U-II only in the length of the N-terminal and is thus a prototype for the ring-system of these hormone peptides. Both the ring-residues Trp-Lys-Tyr and the disulfide bridge are thought to be important for receptor activation [1].
Understanding the dynamic conformational properties of URP can help develop pharmacophores and direct simulations of the receptor.
We describe a 5 µs molecular-dynamics simulation of URP that demonstrates the high flexibility of the peptide. *DASH* [2] analysis reveals several distinct main and transient conformational states that interchange rapidly. These states will be characterized and their properties discussed with some focus on the conformation of the disulfide bridge.

[1] D. Chatenet, T.T. Nguyen, M. Letourneau, A. Fournier, Front Endocrinol, 2012, 3, 7-13
[2] D.W. Salt, B.D. Hudson, L. Banting, M.J. Ellis, M.G. Ford, J Med Chem, 2005, 48, 3214-3220