Clustering analysis of synthetic retinoid docking

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1. Introduction

Retinoids are a class of vitamin-A derived molecules with endogenous roles in cell proliferation and differentiation. Recent research has suggested retinoids may hold promise for therapeutic use in motor neuron diseases such as amyotrophic lateral sclerosis (ALS) by promotion of neuronal survival. Despite promising therapeutic potential, little is known about the complex signalling pathways which govern retinoid's mechanism of action. Endogenous retinoids such as all-trans-retinoic acid (ATRA) are inherently vulnerable to photodegradation and isomerism due to their polyene structure, making their use as a research tool problematic. As such we utilise a range photostable, fluorescent synthetic retinoid analogues we are currently developing between Durham University and LightOx to investigate the retinoid mode of action. In parallel with biological testing, ligand docking and molecular dynamics (MD) simulations form a vital part of our continued research into these compounds. As part of our docking analysis, we have developed a root-mean-square deviation (RMSD)-based clustering script to group and identify commonly occurring ligand-docked protein structures, which we hypothesise will allow for enhanced identification of promising docked solutions via less resource-intensive methods before moving data to resource-intensive MD simulations. This workflow not only introduces a new approach for docking analysis but allows for faster and simpler identification of unique protein-ligand docked solutions.