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Benchmarking Computational Tools for Predicting Absorbance Spectral Shifts in rhodopsin Mutants

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The development of novel optogenetic tools is critically dependent on engineering microbial opsins with red-shifted absorbance spectra, as red light offers superior tissue penetration and reduced phototoxicity compared to blue-green light [1]. To address the resource-intensive nature of site-directed mutagenesis, a number of in silico tools have been introduced to identify promising candidates for experimental validation [2]. However, the predictive performance of these computational tools, ranging from homology-based models to machine learning algorithms and quantum mechanical calculations, remains inadequately assessed against robust experimental datasets for channelrhodopsins [3, 4].

Our work addresses this gap by conducting a systematic comparative analysis of leading predictive tools, benchmarked against a comprehensive set of experimentally determined absorbance maxima for a library of rhodopsin mutants.

We quantitatively evaluate the accuracy, precision, and limitations of each tool in forecasting mutation-induced spectral shifts.Our findings provide practical guidelines for selecting the optimal computational tool and offer a critical cost-benefit analysis of their use, ultimately streamlining the rational design of next-generation, red-shifted rhodopsins for deep-tissue optogenetics.

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References:

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