

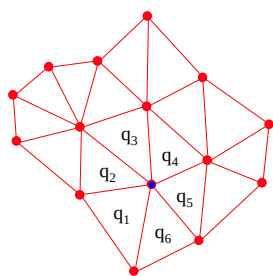
Protein Structure Analysis

Iosif Vaisman

2009

Protein Engineering

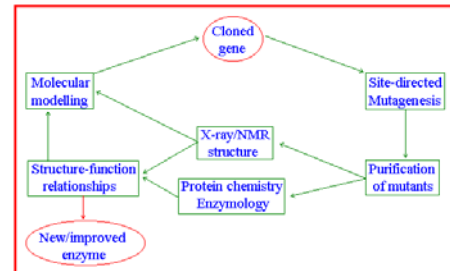
Increase catalytic activity
Change substrate binding site to increase specificity
Change the thermal stability
Increase proteins resistance to proteases
Change codon composition



$$q_{\text{res}} = \sum q_i$$

$$Q_{\text{mut}} = \sum (q_{\text{res}}^{\text{wt}} - q_{\text{res}}^{\text{mut}})$$

Protein Engineering



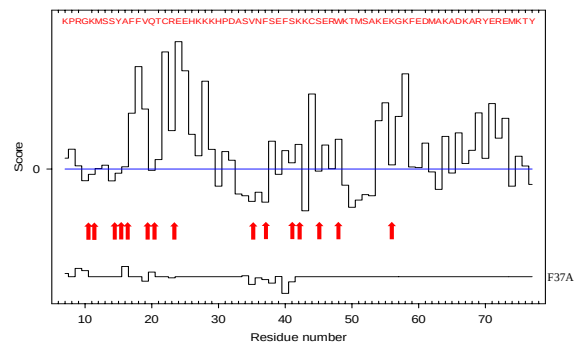
Computational Mutagenesis

Assumption: the structural differences between each mutant and the wild-type protein are usually minor and, therefore, their tessellations are similar

Approach: a single tessellation of either the wild-type or mutant protein structure can be used to develop environmental descriptors for quantitative evaluation of changes in mutant properties

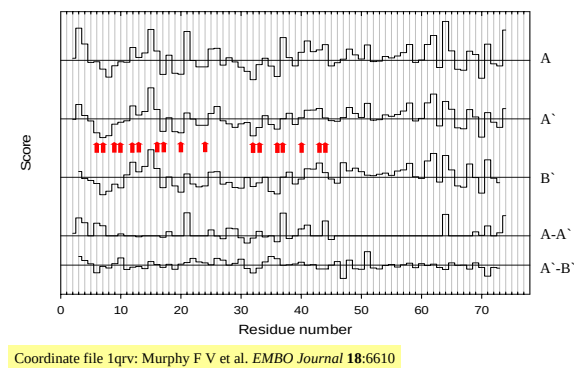
Residue and mutant score

DNA binding residues in HMG1

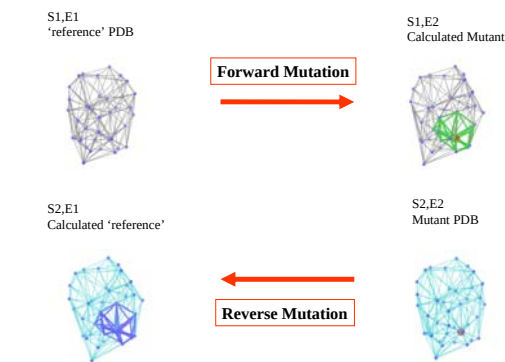


Coordinate file 1ckt: Ohndorf U-M et al. *Nature* 399:708

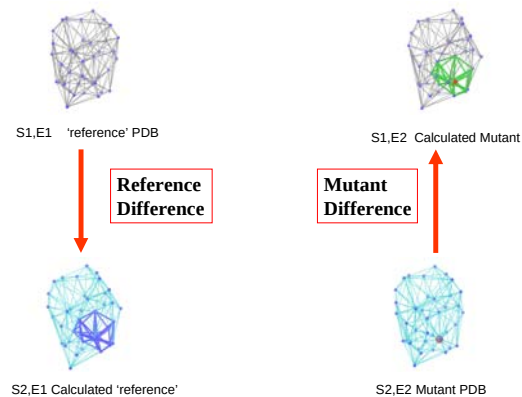
Protein-protein and protein-DNA interfaces (HMG-D)



Reversibility Analysis

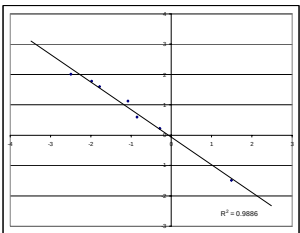


Structural Analysis

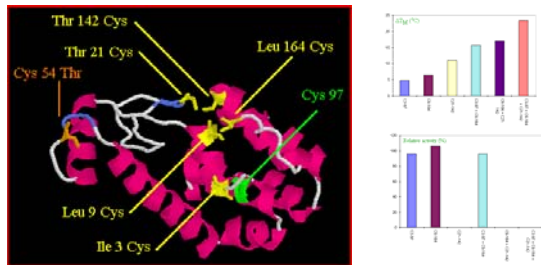


Computational mutagenesis of T4 lysozyme
Reversibility of mutations

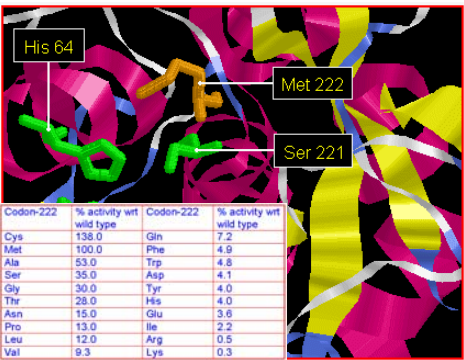
Protein	Mutation	Score change
1163	T26E	-2.49
180l	E26T	2.01
1163	A82S	1.49
123l	S82A	-1.49
1163	V87M	-0.28
1cu3	M87V	0.22
1163	A93C	-1.98
138l	C93A	1.78
1163	T152S	-1.08
190j	S152T	1.12



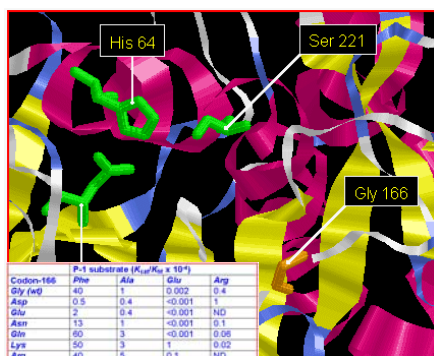
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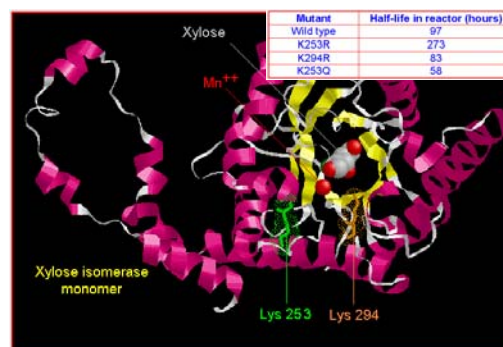
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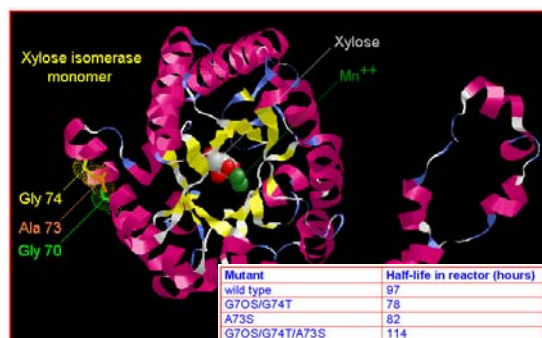
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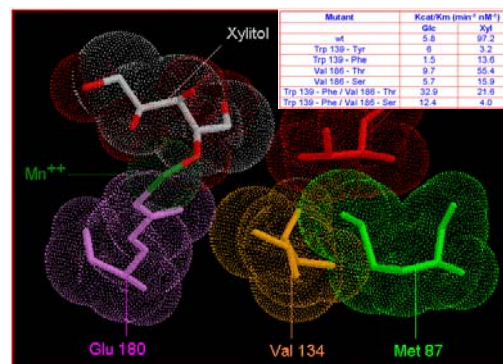
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