GRID/BIOCUBE4mf to rank the influence of mutations on biological processes to design ad hoc mutants

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(Caron et al., 2009)

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Table 1.

box. In particular, for pentalenene synthase we chose “CA” atoms from Phe76, Phe77, Asp80, Asp81,

'

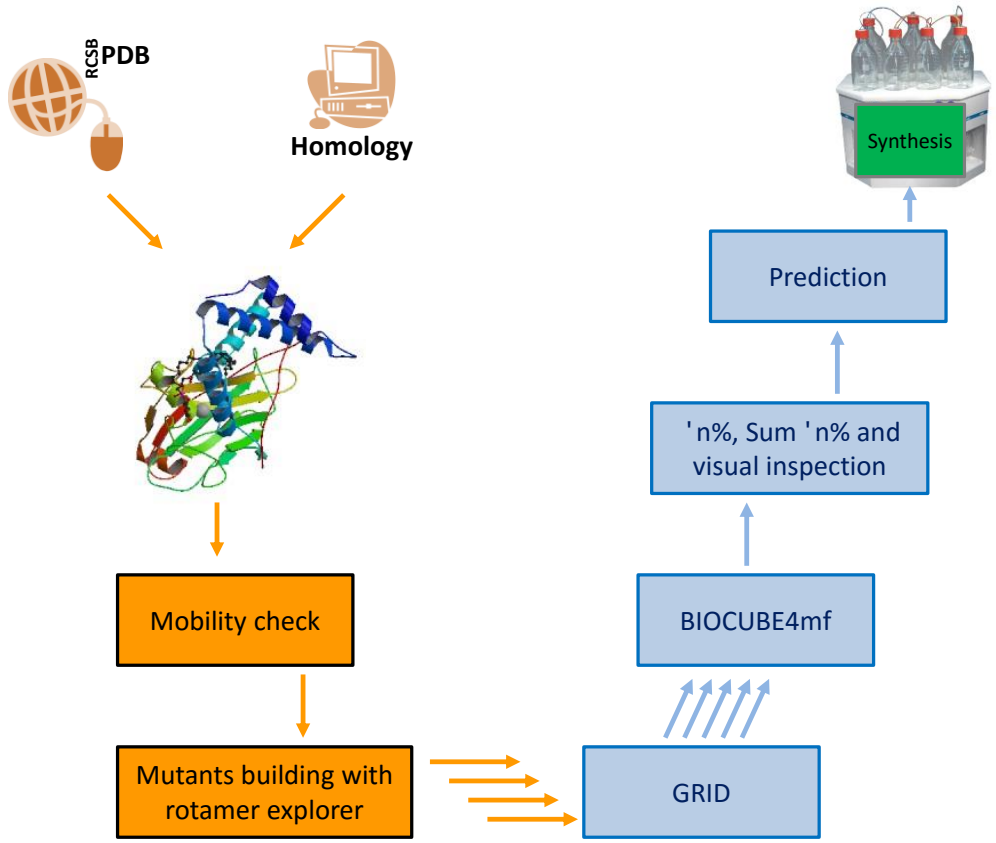
$$' n\% \quad \frac{n_{conf} \quad n_{RS}}{n_{RS}} * 100$$

'

'   '

$$Sum\ ' n\% \quad \sum_{i}\ ' n\%_{i}$$

Figure 1


RCSB PDB
Homology
Synthesis
Prediction
'n%, Sum 'n% and visual inspection
BIOCUBE4mf
GRID
Mobility check
Mutants building with rotamer explorer

Streptomyces

Figure 2

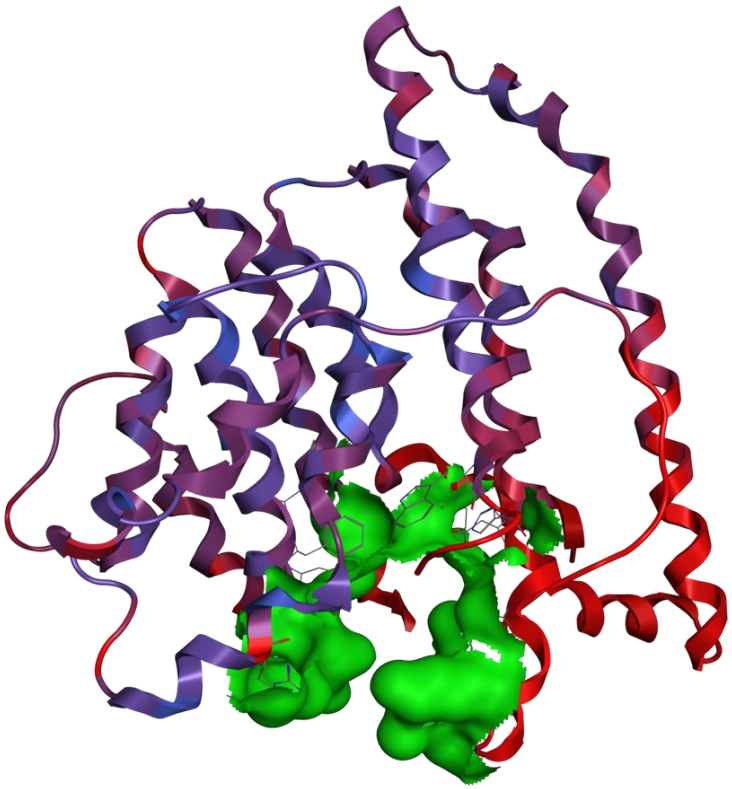


Table 2

RS (WT)	**508**	**211**	**4**	**4**

Table 2 highlights how the flexibility of a side-chain may modulate the mutant interaction profile, and shows the sensitivity of GRID/BIOCUBE4mf to point up these differences.

At the beginning of the study and after a number of tests, it appeared appropriate to use average values of 'n% as final descriptors to take into account the effect of side-chain flexibility. %'n profiles are highly informative, but they are also rather complex to use for comparative purposes. We thus sought a numerical score to facilitate the interpretation of the results. We thus defined the sum of %'n values, including all probes' contribution: Sum%'n (see Methods for definition). Sum%'n were then calculated for the ten mutants and discussed below in relation to the available biological data

The Michaelis constant (measures the concentration of substrate required for significant catalysis to take place. Although K_M is

, i.e the strength of the enzyme-substrate complex (high K_M indicates weak binding and low K_M indicates strong binding).

Table 3. K_M [M] values from Seeman et al. . pK_M (-log K_M) are also reported.

Mutant	**K_M(µM)**	**pK_M**

'

Figure 3. '

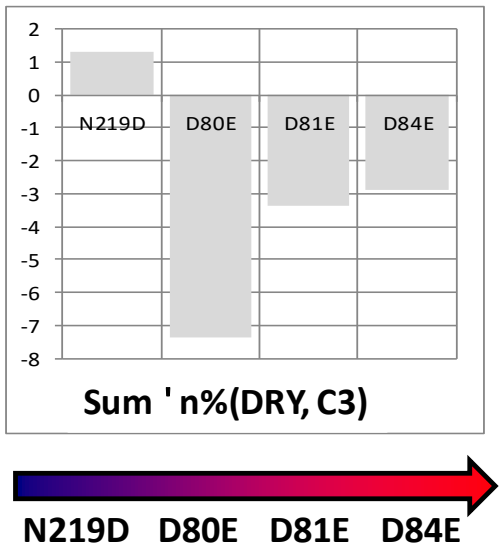

2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
N219D
D80E
D81E
D84E
Sum ' n%(DRY, C3)
N219D D80E D81E D84E

Table 4

In silico

in silico

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