# Using Valence Bond Theory to Model (Bio)Chemical Reactivity

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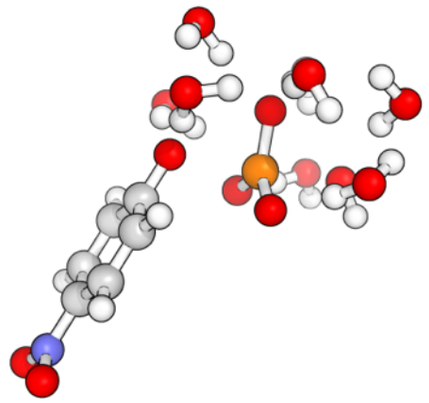
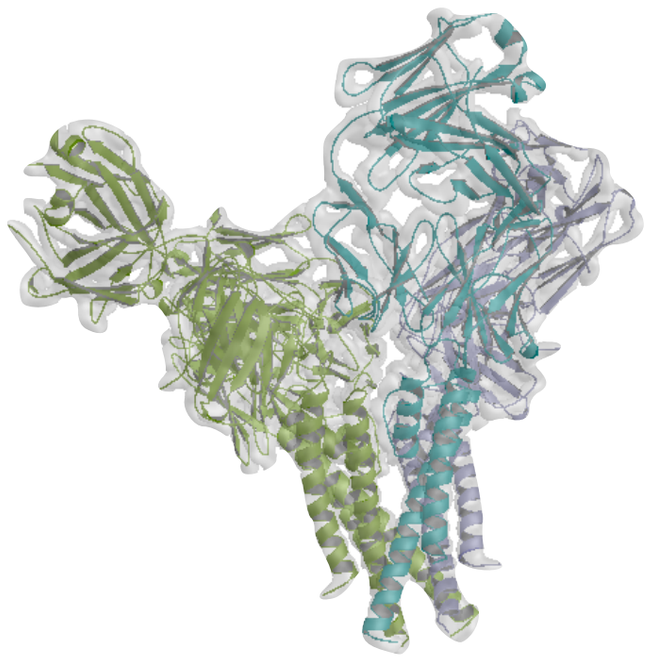
# Motivation

## Quantum Mechanics

Electrons, breaking/forming bond processes, exited state reactions

Computationally demanding ($N^4$-$N^7$): DFT





## Molecular Dynamics

Explicit incorporation of environment effects

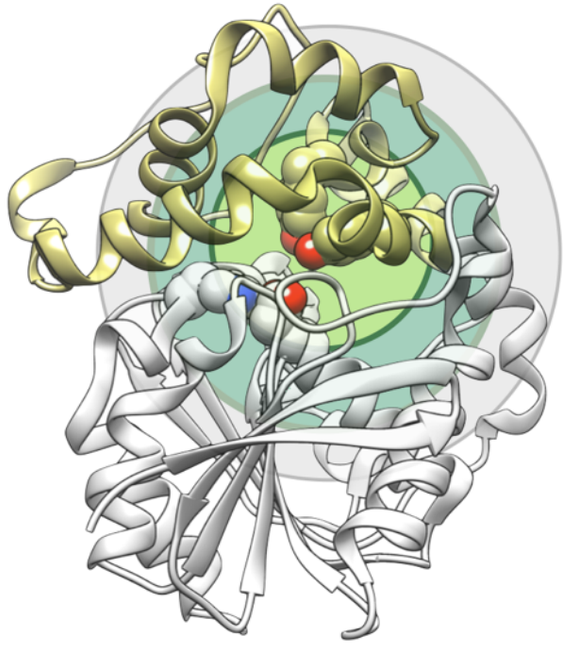
Most FFs (AMBER, OPLSAA, CHARMM) assume the same atomic connectivity throughout simulation. **No Chemistry!!!**

## QM/MM

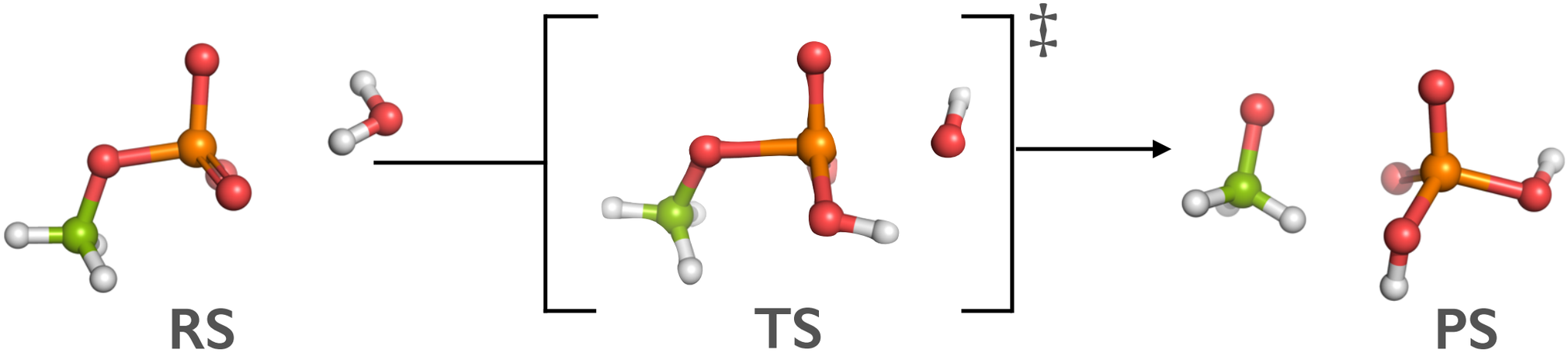
Aims to combine the best of each world...

Sampling/computational cost still an issue

$$E = \left\langle \Psi \middle| \hat{H}^{QM} + \hat{H}_{el}^{QM/MM} \middle| \Psi \right\rangle + E_{van}^{QM/MM} + E^{MM}$$



# Valence Bond (VB) Approach



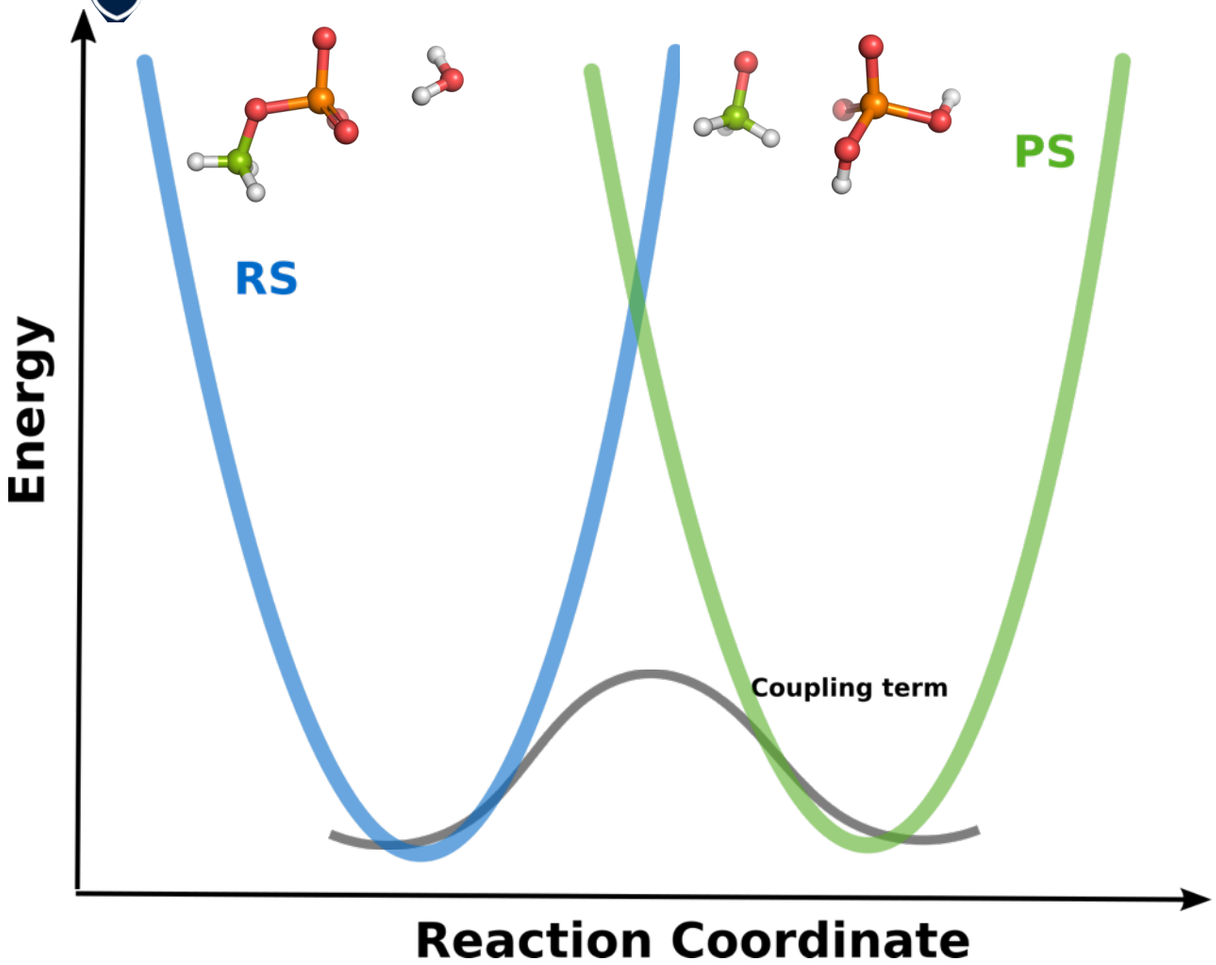

## Valence bond Approach

VB looks for probability of finding a given molecular state

$$\Psi = c_1\psi_1 + c_2\psi_2 + ....c_i\psi_i$$

$$\mathbf{H} = \begin{bmatrix} V_{11} & V_{12} & V_{1j} \\ \vdots & \ddots & \vdots \\ V_{i1} & V_{i2} & V_{ij} \end{bmatrix}$$

# Empirical Valence Bond (EVB)




I) $$\Psi = c_1\psi_1 + c_2\psi_2$$

$$\mathbf{H} = \begin{bmatrix} V_{11} & V_{12} \\ V_{21} & V_{22} \end{bmatrix}$$

$$V_{12} = V_{21} = \langle \psi_1 | \hat{H} | \psi_2 \rangle,$$

$$V_{11} = \langle \psi_1 | \hat{H} | \psi_1 \rangle,$$

$$V_{22} = \langle \psi_2 | \hat{H} | \psi_2 \rangle$$

# Diagonal Elements ($V_{ii}$)/Coupling Element ($V_{ij}$)

$$V_{11} = \langle \psi_1 | \hat{H} | \psi_1 \rangle,$$

$$V_{22} = \langle \psi_2 | \hat{H} | \psi_2 \rangle$$

## Bond Stretch

$$V_{\text{stretch}} = \frac{1}{2} k_R \left( R - R_0 \right)^2 \Longrightarrow V_{\text{stretch}} = D_e \left[ 1 - \exp\left( \beta \left( R - R_0 \right) \right) \right]^2$$

## Non-bonding potentials:

$$V_{\text{Coulomb}} = \frac{q_i q_j e^2}{R_{ij}} \qquad V_{\text{Lennard-Jones}} = \frac{A_{ij}}{R_{ij}^{12}} - \frac{C_{ij}}{R_{ij}^{6}}$$

$$\mathrm{V}_{\text{soft}} = C_i \cdot C_j \cdot e(\text{-}a_i \cdot a_j \cdot r_{i,j})$$

## Bending and Torsional potentials:

$$V_{\text{bend}} = \frac{1}{2} k_\theta \left( \theta - \theta_0 \right)^2 \qquad V_{\text{torsion}} = V_n \left[ 1 + s \cos\left( n\phi \right) \right]; \quad s = \pm 1$$

$$V_{12} = V_{21} = \langle \psi_1 | \hat{H} | \psi_2 \rangle,$$

## Barrier Height

$$V_{12} = A \exp\{-a(r_1 - r_1^0)^2\}$$ Warshel, 1980

$$V_{12} = A \exp\{-(a(r_1 - r_1^0)^2 + 2b(r_1 - r_1^0)(r_2 - r_2^0) + c(r_2 - r_1^0)^2)\}$$

Glowacki, 2011

## Position and frequencies of the TS

$$V_{12} = A \exp\{\mathbf{B}^T \Delta\mathbf{q} - 0.5 \Delta\mathbf{q}^T \cdot C \cdot \Delta\mathbf{q}\}, \quad \Delta\mathbf{q} = \mathbf{q} - \mathbf{q}_{TS}$$

Chang-Miller, 1990

# Potential Energy Surface

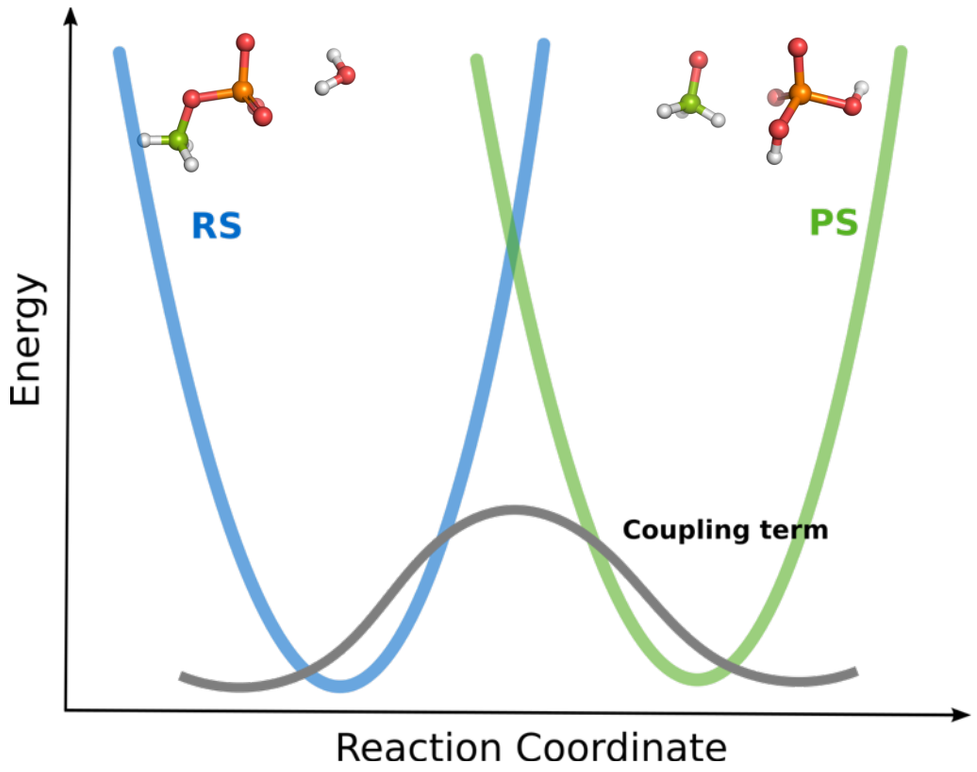
1) $$\Psi = c_1\psi_1 + c_2\psi_2$$

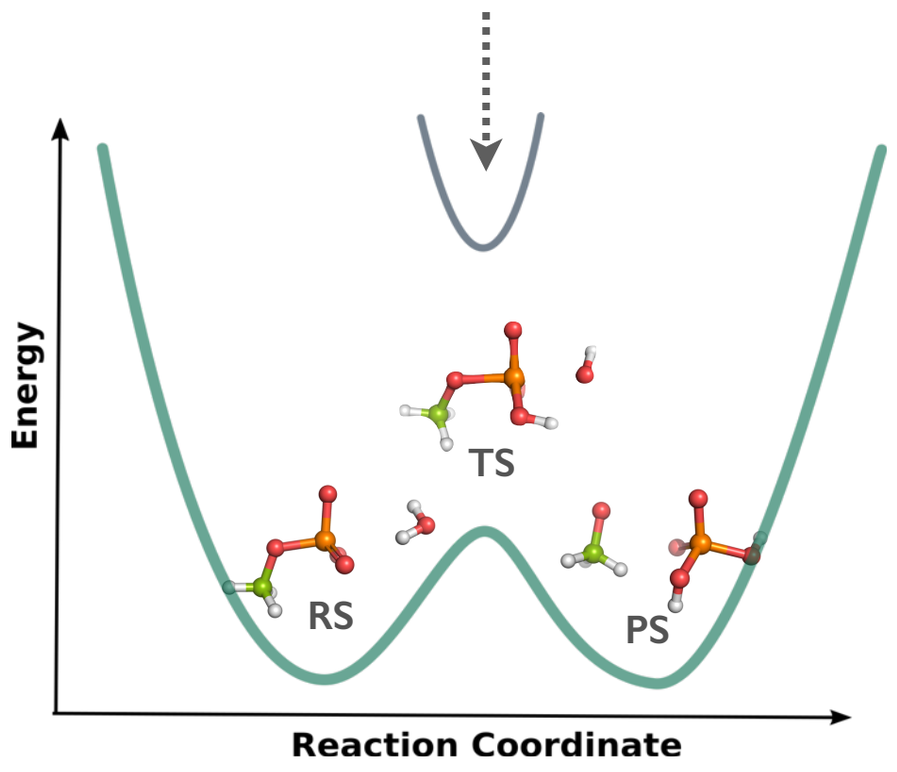
$$\mathbf{H} = \begin{bmatrix} V_{11} & V_{12} \\ V_{21} & V_{22} \end{bmatrix}$$

2) Fit $V_{12}$ to reproduce experimental or (QM) data

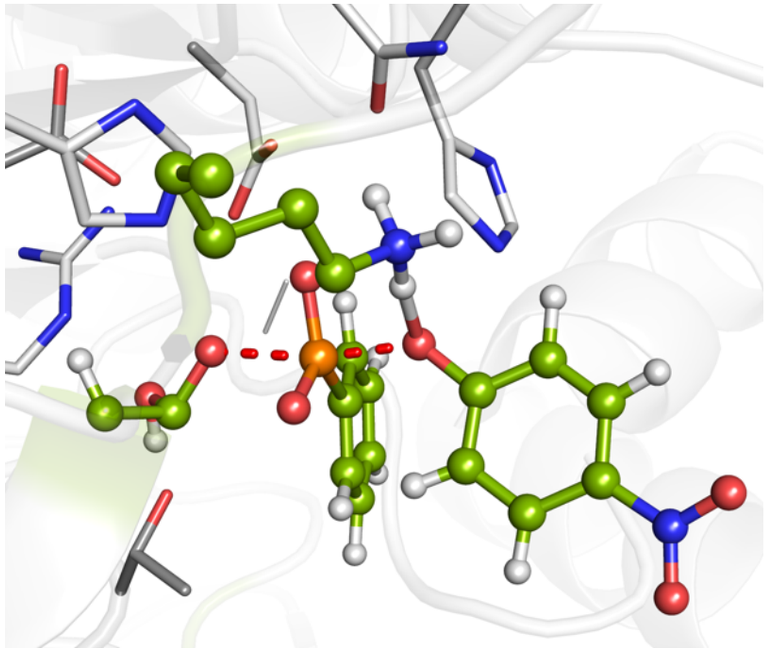
3) Diagonalize V adiabatic states. The minimal value is the ground state.

$$V = {}^1/_2(V_{11} + V_{22}) - \sqrt{[{}^1/_2(V_{11} - V_{22})]^2 + {V_{12}}^2}$$

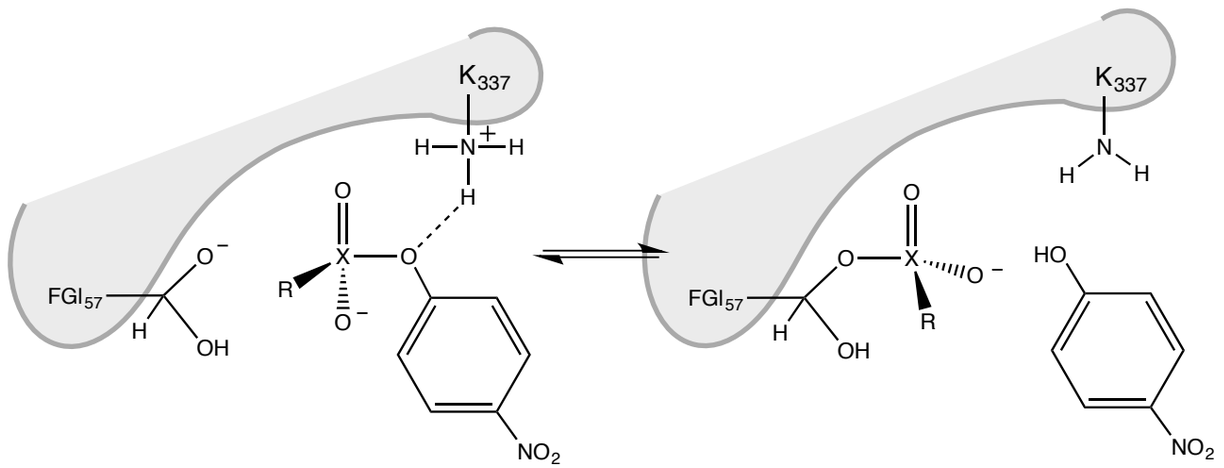


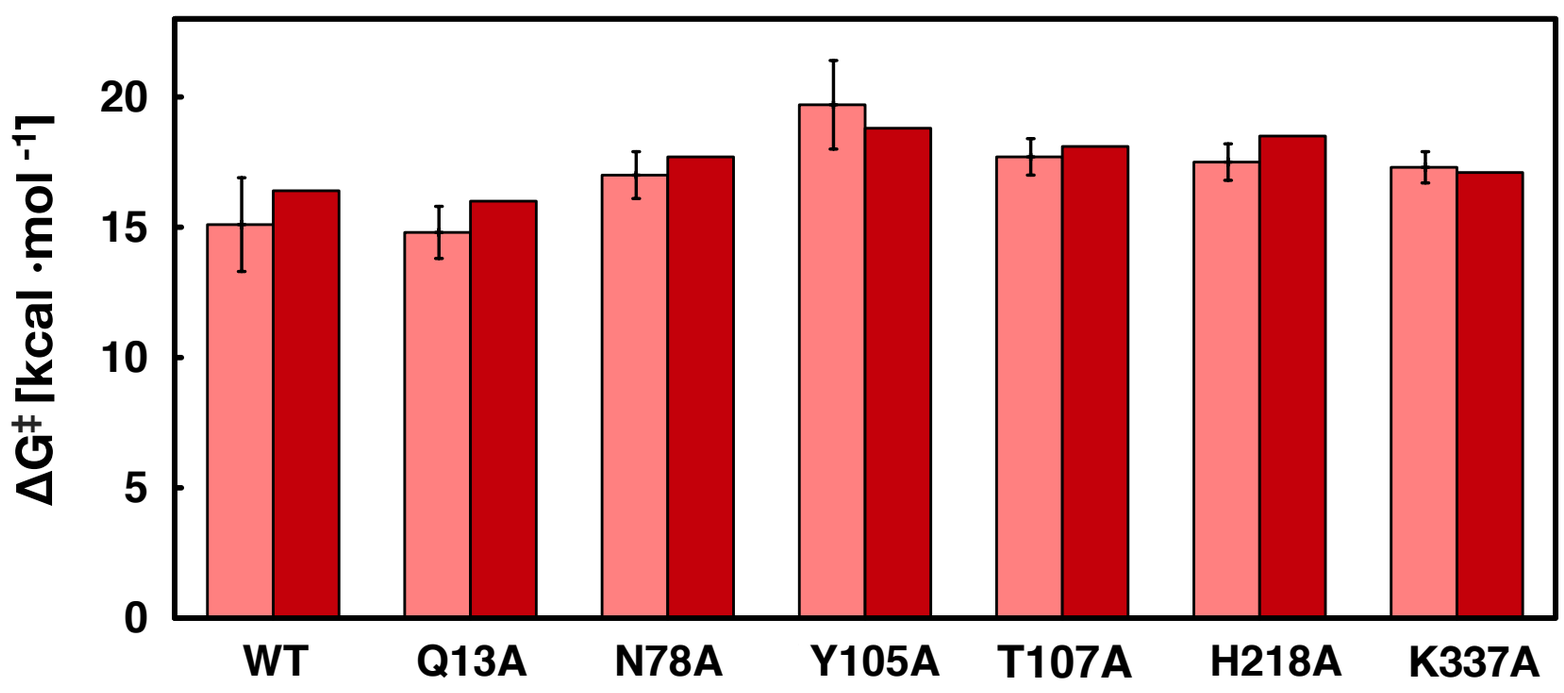



# Empirical Valence Bond (EVB): Enzyme Catalysis



## Phopshate Hydrolysis ($s_N2$ type reaction)






Barrozo/Duarte *et al. J. Am. Chem. Soc.* **2015**, 137, 9061

# Different Flavours of VB

| Program | Capabilities | Website | Comments | Reference |
|---|---|---|---|---|
| **MOLARIS-XG** | EVB, FEP, AC | http://laetro.usc.edu/software.html | Available for purchase from the USC | Warshel and coworkers |
| **Q** | EVB, FEP, LIE | http://xray.bmc.uu.se/~aqwww/q/ | Free for academic use. Available upon request | Åqvist and coworkers |
| **V2000** | VBSCF, BOVB, VBCI, SCVB, CASVB GVB | http://www.scinetec.com | Integrated into GAMESS | McWeeny and coworkers |
| **TURTLE** | VBSCF | http://tc5.chem.uu.nl/ATMOL/turtle/turtle_main.html | Integrated into GAMESS-UK | van Lenthe *et al.* |
| **VM/MM** | VB/MM DE-VB/MM | Available upon request avitalsh@ekmd.huji.ac.il. | Interface program that communicates between XMVB and MOLARIS | Shurki and coworkers |
| **MS-EVB** | MS-EVB | | In house implementation in LAMMPS MD package | Voth and coworkers |
| **AMBER** | Distributed Gaussian EVB | http://ambermd.org/ | AMBER license is required for GPU version | Case and coworkers |
| **XMVB** | VBSCF, BOVB, VBCI, VBPT2, DFVB, VBPCM, VBEFP, VBEFP/PCM | http://ftcc.xmu.edu.cn/xmvb/index.html | Integrated into GAMESS | Wu and coworkers |