

# Some Examples of Bridging Length and Time Scales

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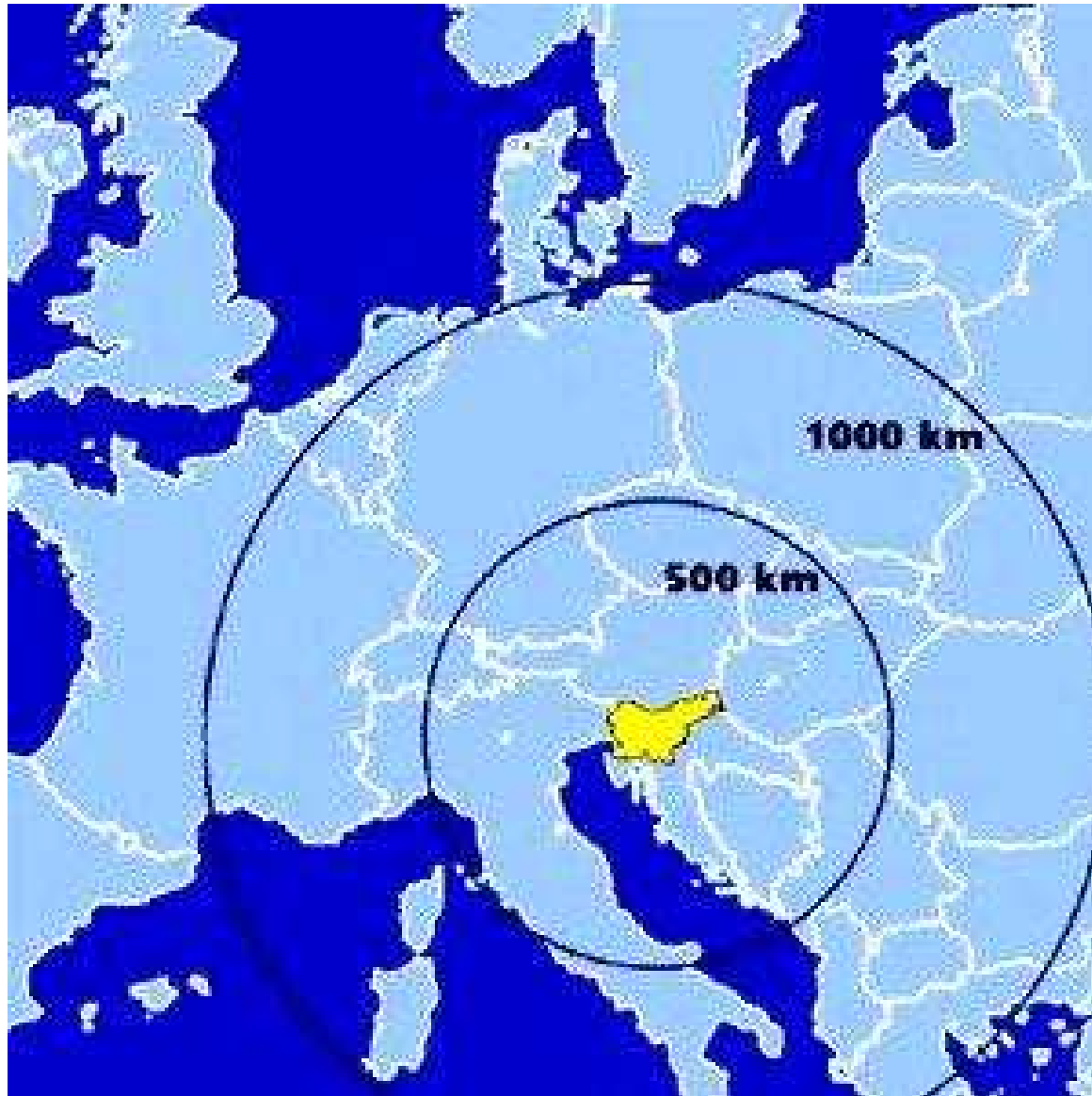
Laboratory for Molecular Modeling

National Institute of Chemistry

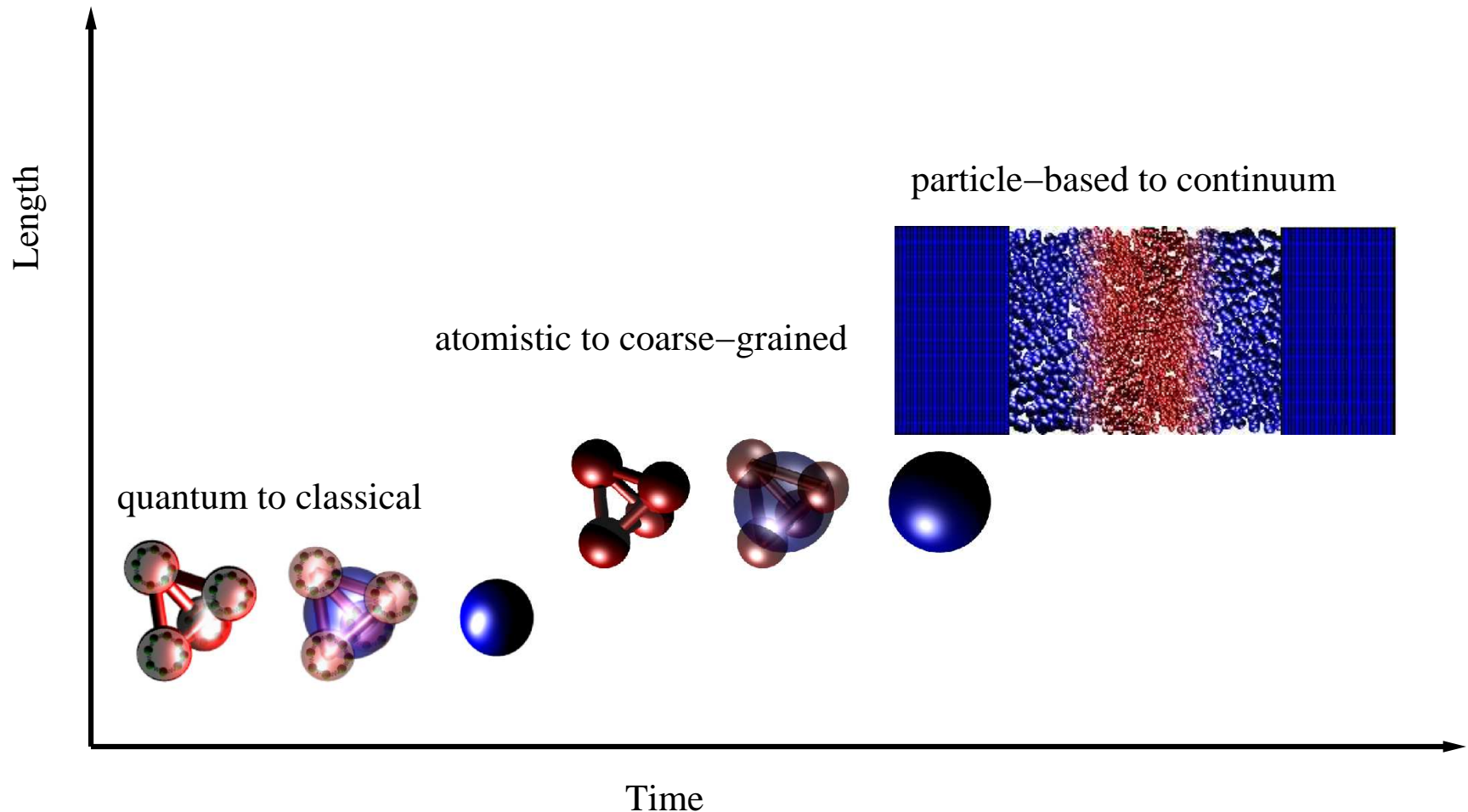
Ljubljana

Slovenia

# Center of Mass Position



# Multiscale Modeling



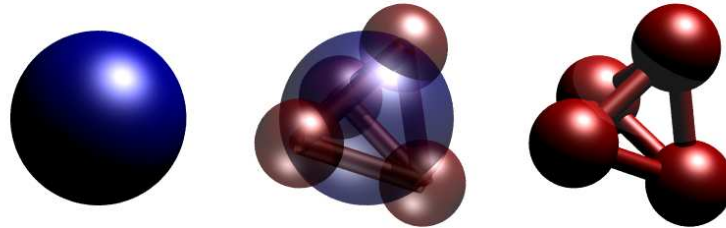
M. Praprotnik, L. Delle Site, Humana Press, 2012.

M. Praprotnik, L. Delle Site, K. Kremer, Annu. Rev. Phys. Chem. **59**, 545 (2008).

M. Praprotnik, S. Poblete, K. Kremer, J. Stat. Phys. **145**, 946-966, 2011.

# Changing Number of DOFs

- A tetrahedral molecule has a defined spatial orientation and  $3N = 12$  DOFs:
  - 3 translational
  - 3 rotational
  - $3N - 6 = 6$  vibrational
- One particle mesoscopic molecule has no defined spatial orientation and only 3 translational DOFs.



M. Praprotnik, L. Delle Site, K. Kremer, J. Chem. Phys. **123**, 224106 (2005).

# AdResS

AdResS consists of two main steps:

1. Derive the effective pair potential  $U^{cm}$  between coarse-grained molecules on the basis of the reference all-atom system.
2. Couple the atomistic and mesoscopic scales:

$$\mathbf{F}_{\alpha\beta} = w(X_\alpha)w(X_\beta)\mathbf{F}_{\alpha\beta}^{atom} + [1 - w(X_\alpha)w(X_\beta)]\mathbf{F}_{\alpha\beta}^{cm},$$

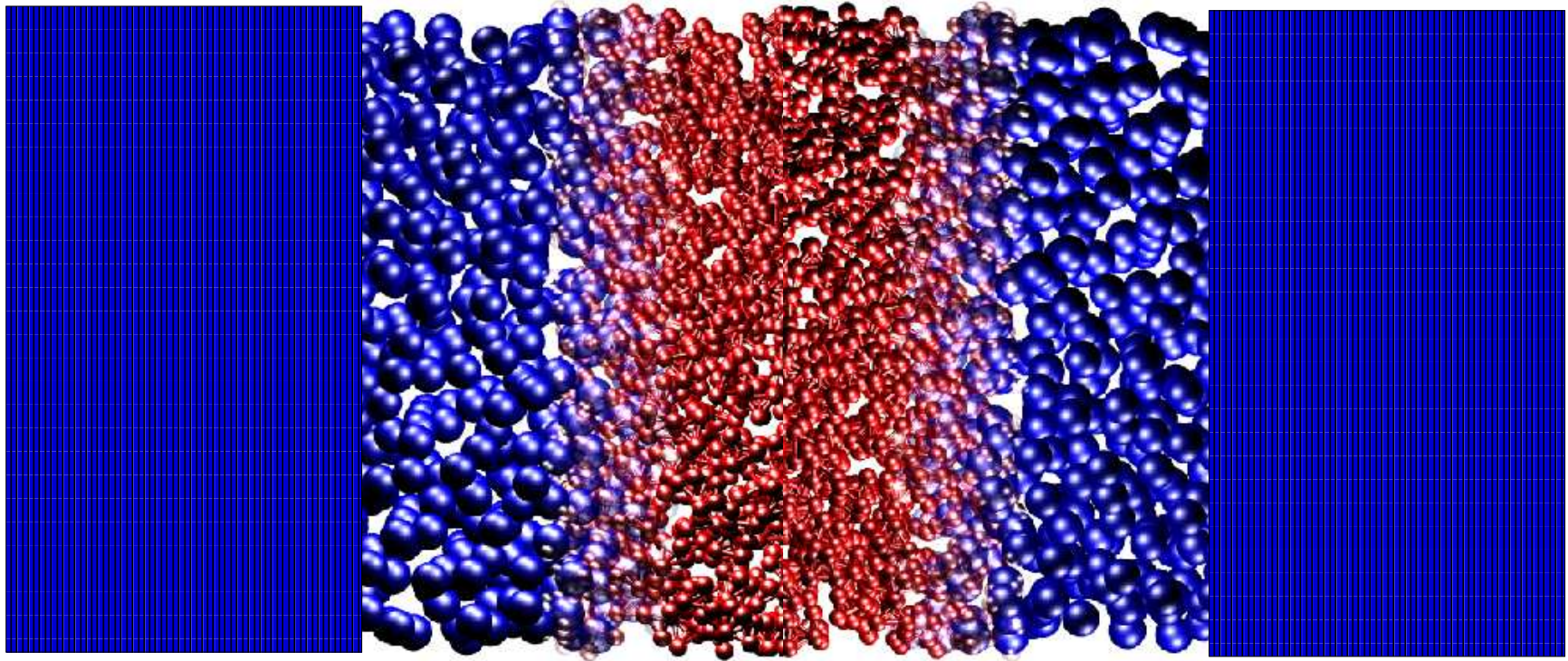
where

$$\mathbf{F}_{\alpha\beta}^{atom} = \sum_{i\alpha, j\beta} \mathbf{F}_{i\alpha j\beta}^{atom}$$

is the sum of all pair interactions between explicit atoms of molecules  $\alpha$  and  $\beta$  and

$$\begin{aligned}\mathbf{F}_{i\alpha j\beta}^{atom} &= -\frac{\partial U^{atom}}{\partial \mathbf{r}_{i\alpha j\beta}}, \\ \mathbf{F}_{\alpha\beta}^{cm} &= -\frac{\partial U^{cm}}{\partial \mathbf{R}_{\alpha\beta}}.\end{aligned}$$

# Coupling MD with Continuum



$$\mathbf{J} = p \mathbf{I} + \rho \mathbf{v} \mathbf{v} + \mathbf{\Pi}$$

R. Delgado Buscalioni, K. Kremer, M. Praprotnik, J. Chem. Phys. **128**, 114110 (2008).

R. Delgado Buscalioni, K. Kremer, M. Praprotnik, J. Chem. Phys. **131**, 244107, (2009).

# Navier-Stokes Equation

**Conservation of momentum:**

$$\rho \left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \nabla \cdot \mathbf{\Pi} + \mathbf{f}$$

**Stress tensor:**

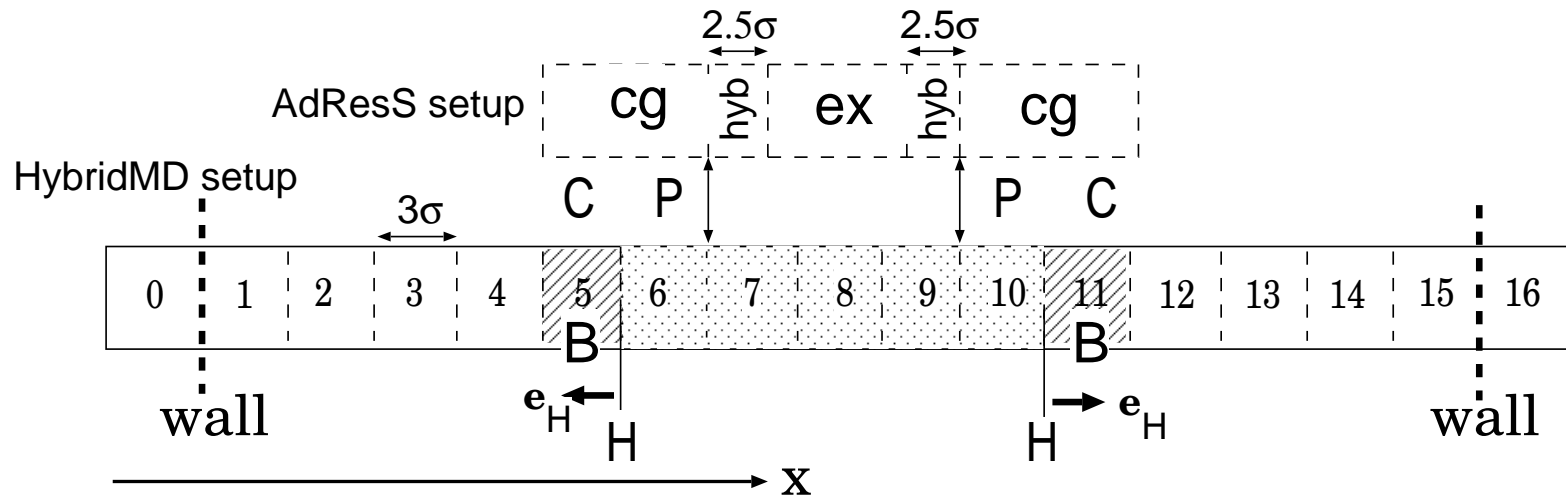
$$\mathbf{\Pi} = -\eta [\nabla \mathbf{u}]^S - \xi \nabla \cdot \mathbf{u} \mathbf{I}$$

We consider a Newtonian fluid with dynamic viscosity  $\eta$  and bulk viscosity  $\xi$ . The traceless symmetric tensor is defined as  $A_{\alpha\beta}^S = (A_{\alpha\beta} + A_{\beta\alpha}) - (2/3)A_{\gamma\gamma}$ .

**Conservation of mass:**

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{u}) = 0$$

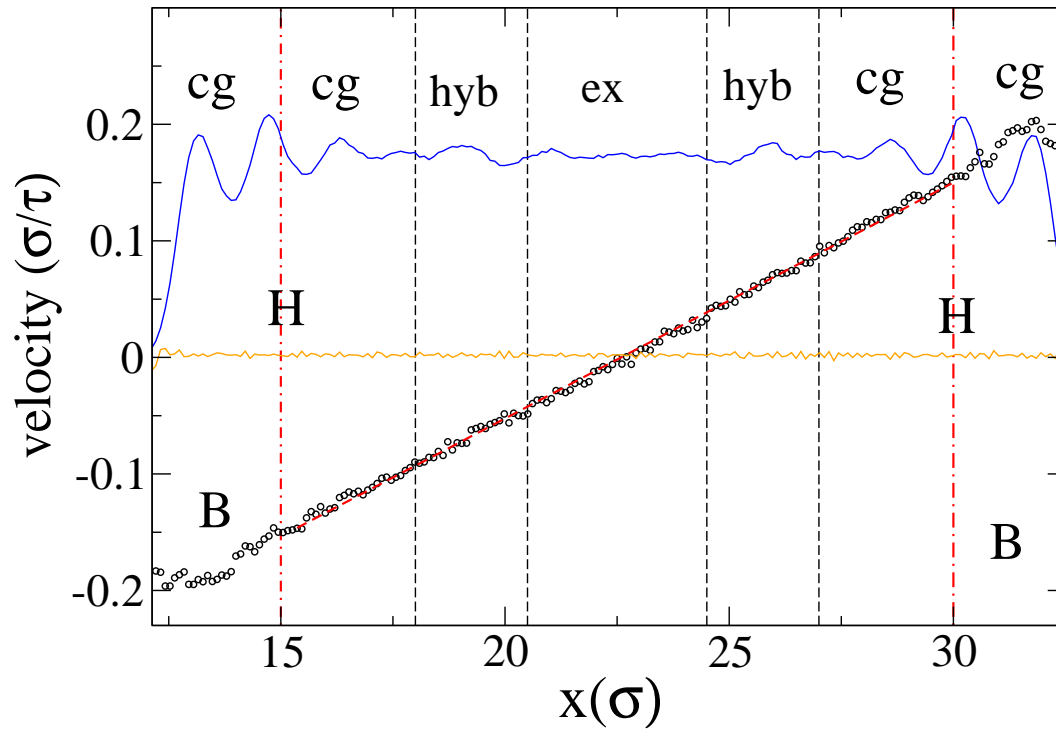
# Triple-Scale Scheme



- Domain decomposition of the combined scheme.

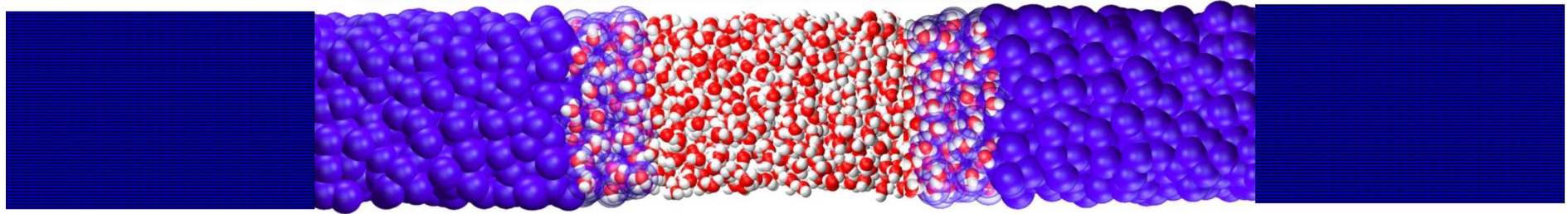
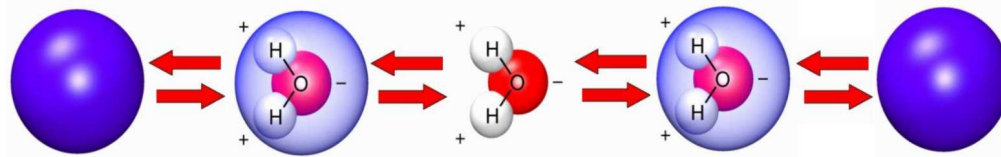


# Couette Flow



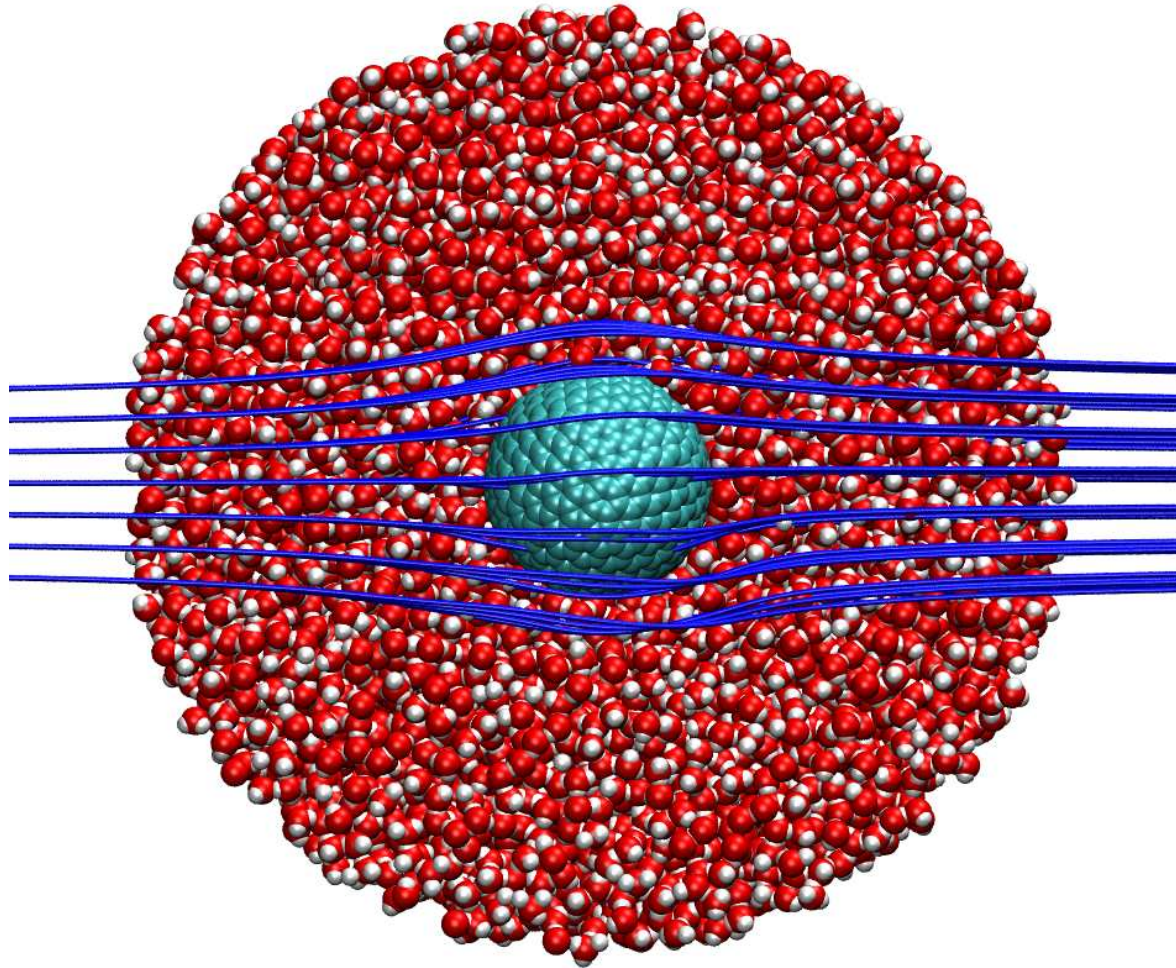
- Velocity profile at the particle region of an hybrid simulation of a Couette flow.

# Triple-Scale Simulation: Liquid Water



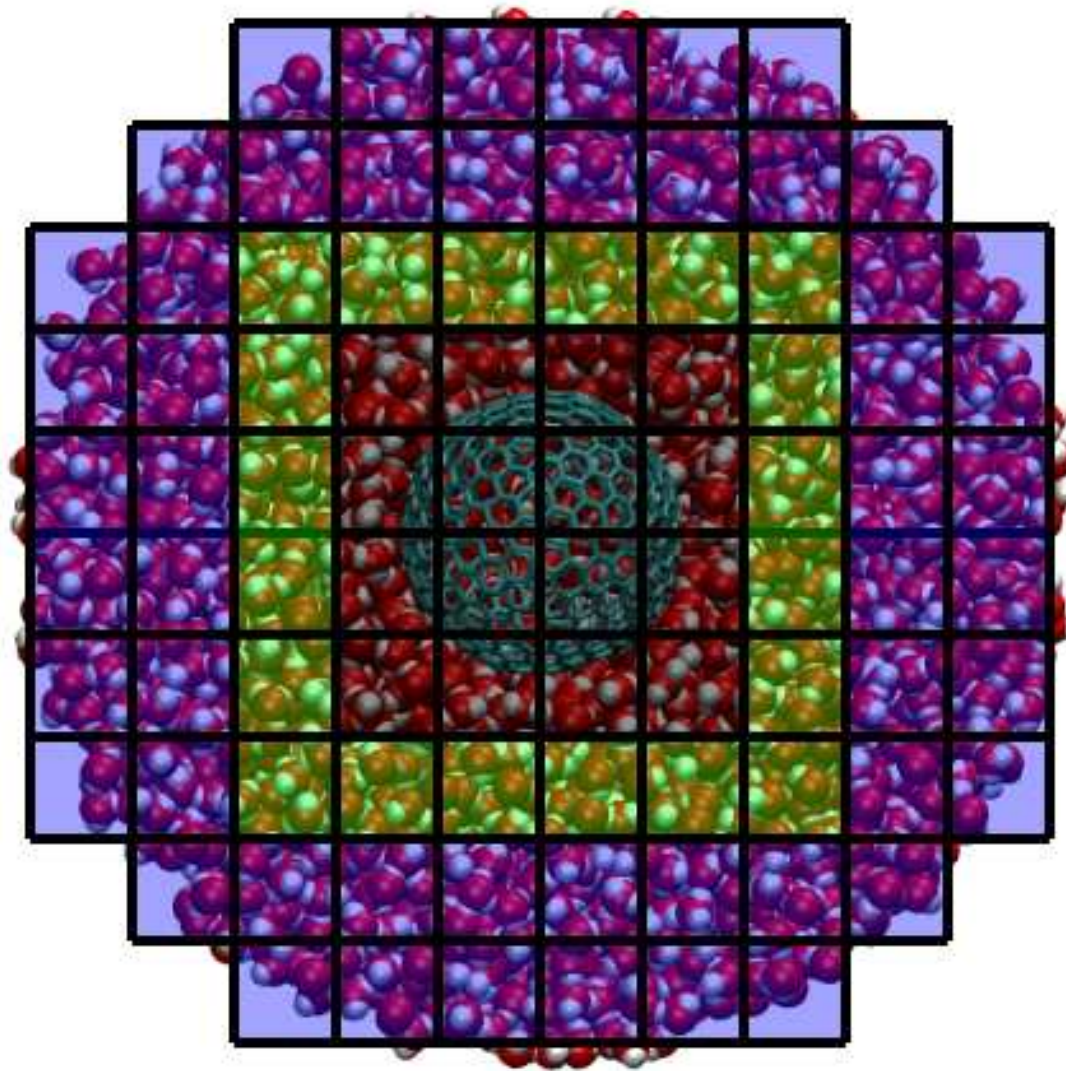
R. Delgado Buscalioni, K. Kremer, M. Praprotnik, J. Chem. Phys. **131**, 244107, (2009).

# Multiscale Flow past a Buckyball



J. H. Walther, M. Praprotnik, E. M. Kotsalis, P. Koumoutsakos, *J. Comput. Phys.* **231**, 2677-2681, 2012.

# Overlap Domain



Cross-section through the overlap region.

# Fractional DOFs

- For the fractional quadratic DOF  $\Theta$  with the weight  $w = \alpha$  we can write the **partition function** as:

$$\begin{aligned}\exp(-\beta F_\alpha) &= C \int \exp(-\beta \alpha p_\Theta^2 / 2) dV_\alpha = \\ &= 2C \int_0^\infty \exp(-\beta \alpha p_\Theta^2 / 2) |p_\Theta|^{\alpha-1} \frac{dp_\Theta}{\Gamma(\alpha)} = \\ &= \frac{2^{\alpha/2} C \Gamma(\alpha/2)}{\Gamma(\alpha)} \alpha^{-\alpha/2} \beta^{-\alpha/2} \sim \beta^{-\alpha/2}.\end{aligned}$$

- $\langle K_\alpha \rangle = \frac{d(\beta F_\alpha)}{d\beta} = \frac{\alpha}{2\beta} = \frac{\alpha k_B T}{2}.$

- In equilibrium  $T_A = T_B = T_\Delta = T$  and thus:  $n_\alpha \sim \alpha.$

M. Praprotnik, K. Kremer, L. Delle Site, Phys. Rev. E **75**, 017701 (2007).

M. Praprotnik, K. Kremer, L. Delle Site, J. Phys. A: Math. Theor. **40**, F281, 2007.

# MD Integration

$$\frac{d\boldsymbol{\eta}}{dt} = \{\boldsymbol{\eta}, H\} = \hat{L}_H \boldsymbol{\eta}$$

$\hat{L}_H = \{ \cdot, H \}$  is the Lie operator

$H$  is the Hamiltonian

$\{\boldsymbol{\eta}, H\}$  denotes the Poisson bracket

$\boldsymbol{\eta} = (\mathbf{q}, \mathbf{p})$  is a vector in phase space composed of the momenta and coordinates of all particles

**Formal solution:**

$$\boldsymbol{\eta}|_{t+\Delta t} = \exp(\Delta t \hat{L}_H) \boldsymbol{\eta}|_t$$

$\Delta t$  is the integration time step

$\exp(\Delta t \hat{L}_H)$  is defined as a formal series of operators

# SISM

We split the Hamiltonian function as

$$H = H_0 + H_r$$

We then use the following approximation:

$$\boldsymbol{\eta}|_{t+\Delta t} = \exp\left(\frac{\Delta t}{2}\hat{L}_{H_0}\right)\exp(\Delta t\hat{L}_{H_r})\exp\left(\frac{\Delta t}{2}\hat{L}_{H_0}\right)\boldsymbol{\eta}|_t + \mathcal{O}(\Delta t^3)$$

$\Delta t$  is the integration time step.

M. Praprotnik, D. Janezic, J. Chem. Inf. Model. **45**, 1571-1579, 2005.

D. Janezic, M. Praprotnik, F. Merzel, J. Chem. Phys. **122**, 174101, 2005.

M. Praprotnik, D. Janezic, J. Chem. Phys. **122**, 174102, 2005.

M. Praprotnik, D. Janezic, J. Chem. Phys. **122**, 174103, 2005.

**Step 0:** Perform the analysis of normal modes of the harmonical part  $H_0$ .

**Step 1:** Propagate with  $H_0$  for the time  $\Delta t/2$ .

$$\begin{bmatrix} P'_i \\ Q'_i \end{bmatrix} = \begin{bmatrix} \cos(\omega_i \frac{\Delta t}{2}) & -\omega_i \sin(\omega_i \frac{\Delta t}{2}) \\ \frac{1}{\omega_i} \sin(\omega_i \frac{\Delta t}{2}) & \cos(\omega_i \frac{\Delta t}{2}) \end{bmatrix} \begin{bmatrix} P_i^0 \\ Q_i^0 \end{bmatrix}$$

$$P'_i = P_i^0$$

$$Q'_i = P_i^0 \frac{\Delta t}{2} + Q_i^0$$

**Step 2:** Transformation

$$p'_i = \sqrt{m_i} \sum_k \mathbf{A}_{ik} P'_k$$

$$q'_i = \frac{1}{\sqrt{m_i}} \sum_k \mathbf{A}_{ik} Q'_k$$

**Step 3:** Evolve with  $H_r$  for the time  $\Delta t$ .

$$p''_i = p'_i - \Delta t \left( \frac{\partial H_r}{\partial q_i} \right)_{q_i=q'_i}$$

$$q''_i = q'_i + \Delta t \left( \frac{\partial H_r}{\partial p_i} \right)_{p_i=p'_i} = q''_i$$

**Step 4:** Back transformation

$$P''_i = \sum_k \frac{1}{\sqrt{m_k}} \mathbf{A}_{ik}^T p''_k$$

$$Q''_i = \sum_k \sqrt{m_k} \mathbf{A}_{ik}^T q''_k$$

**Step 5:** Propagate with  $H_0$  for the time  $\Delta t/2$ .

$$\begin{bmatrix} P_i \\ Q_i \end{bmatrix} = \begin{bmatrix} \cos(\omega_i \frac{\Delta t}{2}) & -\omega_i \sin(\omega_i \frac{\Delta t}{2}) \\ \frac{1}{\omega_i} \sin(\omega_i \frac{\Delta t}{2}) & \cos(\omega_i \frac{\Delta t}{2}) \end{bmatrix} \begin{bmatrix} P''_i \\ Q''_i \end{bmatrix}$$

**Step 6:** Return to **step 1** until the desired number of calculation steps is completed.



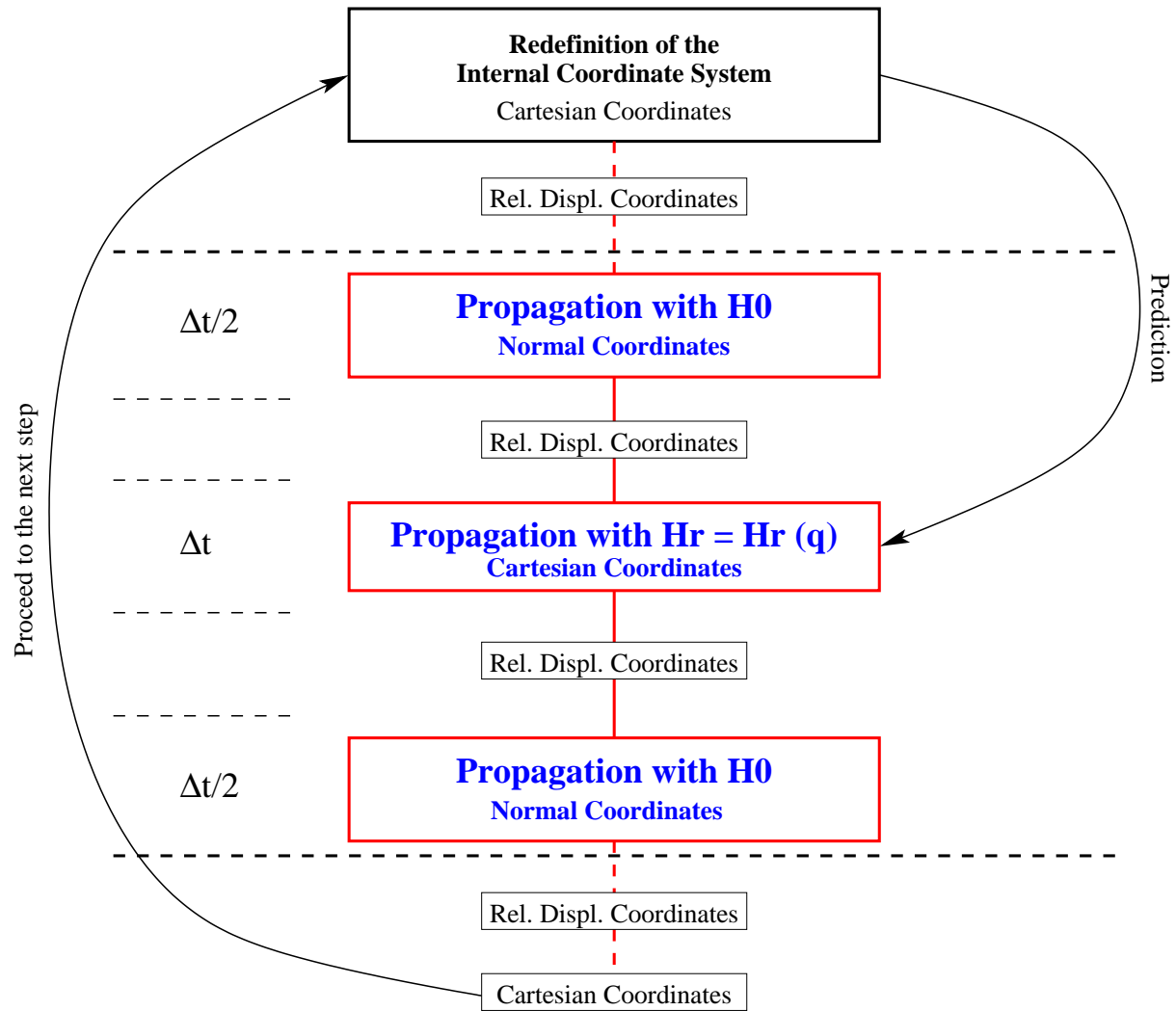
# Time Reversibility

Because of the time reversibility

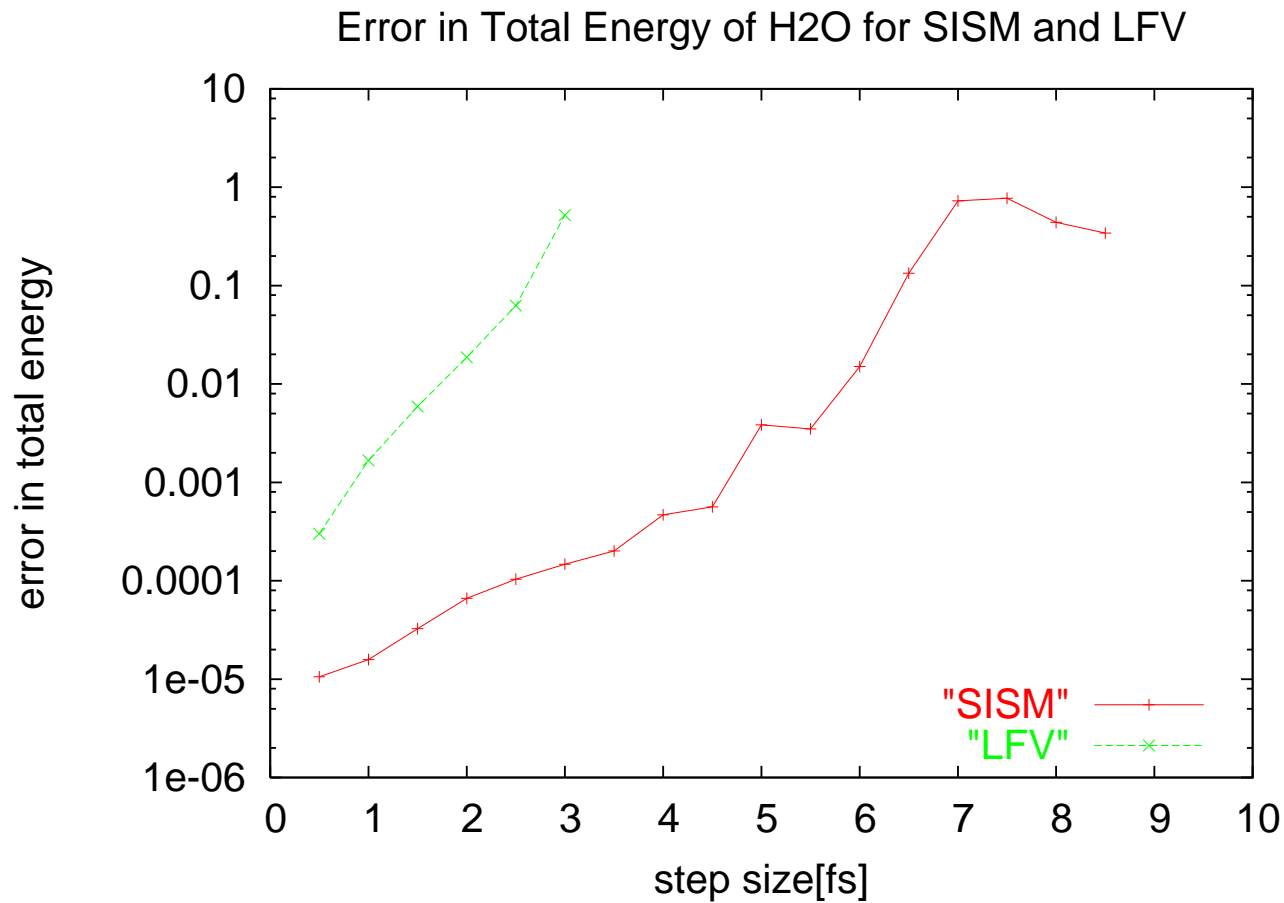
$$\exp\left(\Delta t \hat{L}_H\right) \exp\left(-\Delta t \hat{L}_H\right) = \mathbf{I}$$

the equations used in the numerical method must be time reversible.

# SISM Scheme

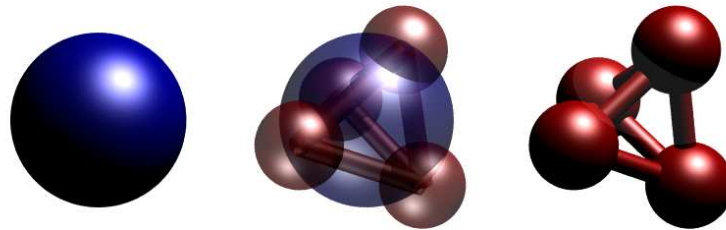


# Error in Energy



# Adaptive Resolution

- A tetrahedral molecule has a defined spatial orientation and  $3N = 12$  DOFs:
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- One particle mesoscopic molecule has no defined spatial orientation and only 3 translational DOFs.



M. Praprotnik, L. Delle Site, K. Kremer, J. Chem. Phys. **123**, 224106 (2005).



Enzyme Kinetics

- Reaction Scheme
- Set Parameters
- Project Setup
- Help

**Differential Equations**

```
dSES/dt = +k6*ES*S-k7*SES-k10*SES
dE/dt = -k0*E*S+k1*SE+k5*EA
dSE/dt = +k0*E*S-k1*SE-k2*SE+k3*ES+k11*SEA
dEAS/dt = +k12*SEA-k13*EAS-k14*EAS*S+k15*SEAS
dEA/dt = +k4*ES-k5*EA-k8*EA*S+k9*SEA
dSEAS/dt = +k14*EAS*S-k15*SEAS
dP/dt = +k10*SES+k4*ES
dES/dt = +k2*SE-k3*ES-k4*ES-k6*ES*S+k7*SES
dS/dt = +k15*SEAS-k14*EAS*S+k9*SEA-k8*EA*S+k7*SES-k6*ES*S-k
dSEA/dt = +k8*EA*S-k9*SEA+k10*SES-k11*SEA-k12*SEA+k13*EAS
```

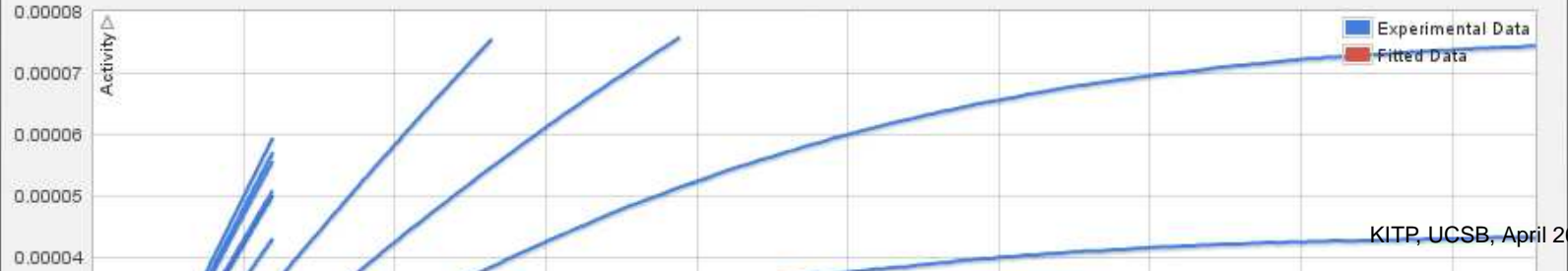
Reset Field

**Evaluated Parameters** [\(Show Fitting Tips\)](#)

Start Stop

- Rate Constants
- Experimental Data
- Evaluation Options

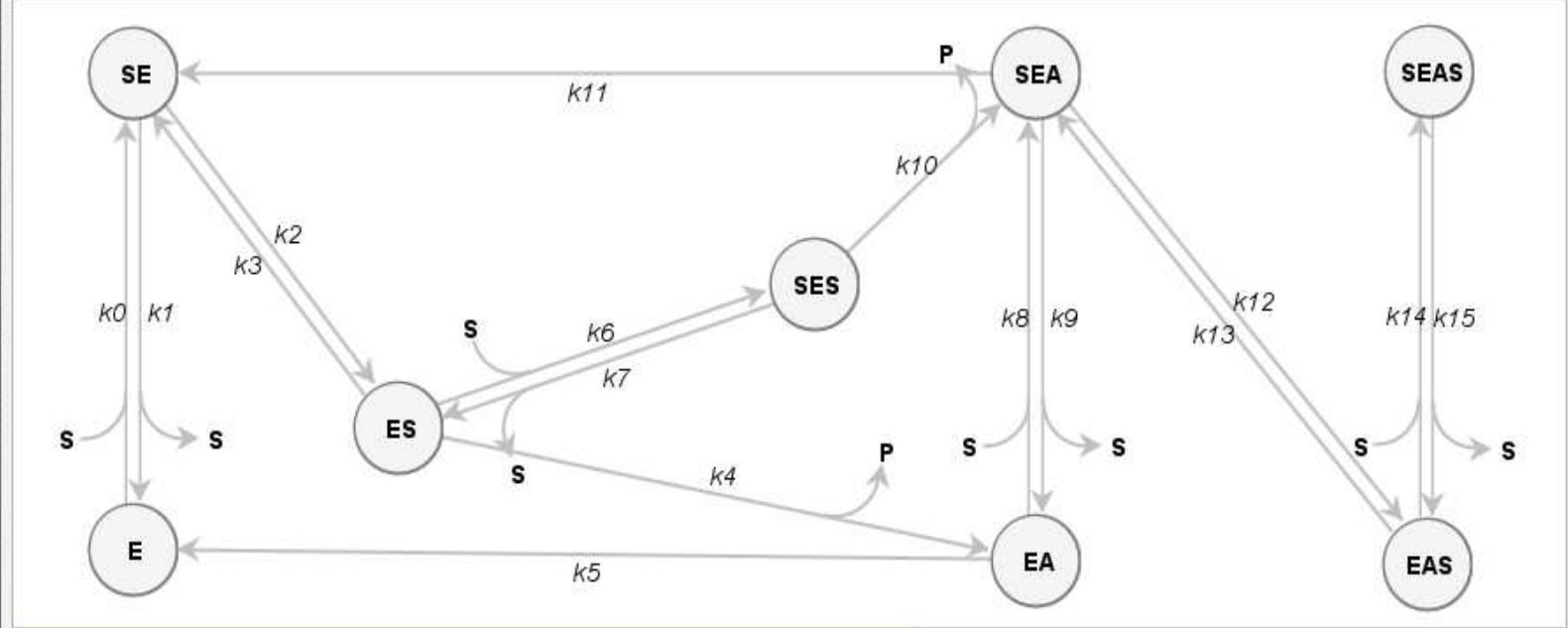
Time Course of the Reaction





Reaction Scheme    Set Parameters    Project Setup    Help

Node    Connect    Move/Select    Arc In    Arc Out    Delete    Clear Scheme    Save    Load



Node tool: Click to create node, then type to set label. Press backspace key to delete label.





Enzyme Kinetics

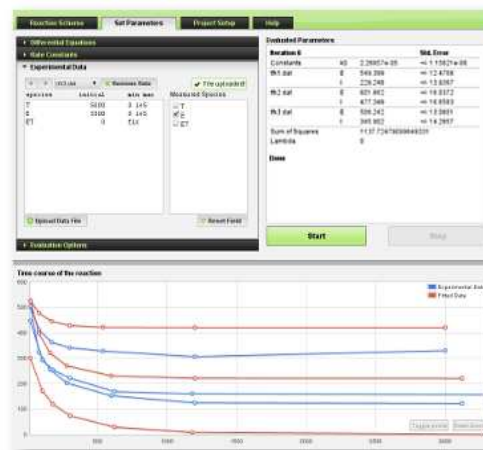
## Introduction: What is ENZO?

ENZO is a web tool for easy construction and quick testing of kinetic models of enzyme catalyzed reactions.

The tool can be utilized by any interested researcher for efficient testing and evaluation of various kinetic models for a given enzyme catalyzed reaction.

No installation or registration is required. It works on any operating system with a modern browser and Java installed.

**Test kinetic models in just 3 steps.**



Introduction Step 1 Step 2 Step 3



Quick Guide



Start Using



Examples

Citing: Bevc S, Konc J, Stojan J, Hodošček M, Penca M, Praprotnik M, Janežič D (2011) ENZO: a Web Tool for Derivation and Evaluation of Kinetic Models of Enzyme Catalyzed Reactions. PLoS ONE 6(7): e22265. doi: 10.1371/journal.pone.0022265 [Open Access](#)

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