# A PHASE-FIELD APPROACH IN MODELING IMPLICIT SOLVATION SYSTEM WITH ELECTROSTATICS

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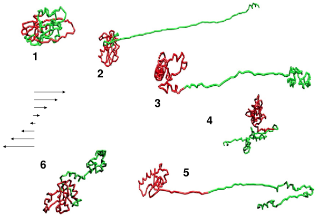
# Overview

1. Modeling
2. Numerical Methods
3. Numerical Results
4. Future Work

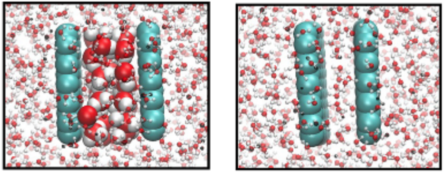
# Modeling

# Implicit Solvent Model

Protein folding, assembling, conformational change

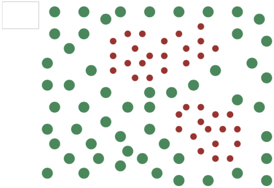


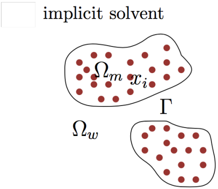

P. Szymczak and M. Cieplak, J. Phys.: Condens. Matter, 23:033102, 2011.



J. A. Morrone and J. Li and B. Berne, J. Phys. Chem. B, 116, 11537-11544, 2012.

# PF - VISM model






- PF-VISM Solvation Free Energy

$$F^{\epsilon}[\phi] = \gamma \int_{\Omega} \left[ \frac{\epsilon}{2} |\nabla \phi|^2 + \frac{1}{\epsilon} W(\phi) \right] \mathrm{d}\mathbf{x} + \rho_w \int_{\Omega_w} f(\phi) U_{vdW} \mathrm{d}\mathbf{x} + \int_{\Omega_w} f(\phi) U_{ele} \mathrm{d}\mathbf{x}$$

$$U_{vdW} = 4\epsilon_i \left[ \left( \frac{\sigma_i}{r} \right)^{12} - \left( \frac{\sigma_i}{r} \right)^{6} \right], \quad U_{ele} = \frac{1}{32\pi^2 \epsilon_0} \left( \frac{1}{\epsilon_m} - \frac{1}{\epsilon_w} \right) \left| \sum_{i=1}^{N} \frac{Q_i(\mathbf{x} - \mathbf{x}_i)}{|\mathbf{x} - \mathbf{x}_i|^3} \right|^2$$

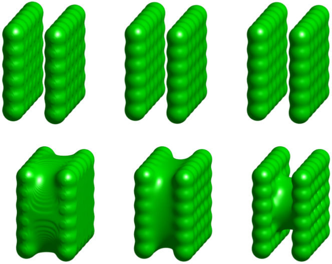

- Y. Zhao, Y-Y Kwan, J. Che, B. Li, and J. A. McCammon, J. Chem. Phys., 139:024111, 2013.
- H. Sun, J. Wen, Y. Zhao, B. Li, and J. A. McCammon, J. Chem. Phys., 143:243110, 2015.
- B. Li and Y. Zhao, SIAM J. Applied Math., 73:1–23, 2013.
- S. Dai and B. Li and J. Lu, Arch. Rational Mech. Anal., 227(1):105–147, 2018.

# PF - VISM model

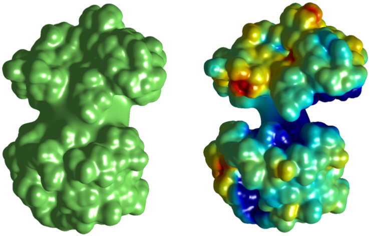
- Gradient flow:

$$\partial_t \phi = -\frac{\delta F^\epsilon}{\delta \phi}[\phi] = \gamma \left[ \epsilon \Delta \phi - \frac{1}{\epsilon} W'(\phi) \right] - f'(\phi)(\rho_w U_{vdW} + U_{ele})$$

$$W(\phi) = 18(\phi^2 - \phi)^2 \, , \qquad f(\phi) = (\phi - 1)^2$$



H. Sun, J. Wen, Y. Zhao, B. Li, and J. A. McCammon, J. Chem. Phys., 143:243110, 2015.



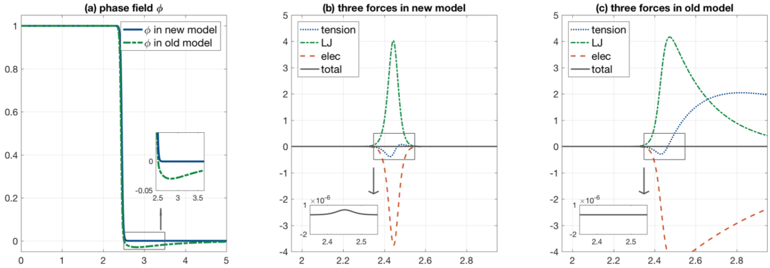
H. Sun, J. Wen, Y. Zhao, B. Li, and J. A. McCammon, J. Chem. Phys., 143:243110, 2015.

# An improved PF - VISM model

- Gradient flow:

$$\partial_t \phi = -\frac{\delta F^{\epsilon}}{\delta \phi}[\phi] = \gamma \left[ \epsilon \Delta \phi - \frac{1}{\epsilon} W'(\phi) \right] - f'(\phi)(\rho_w U_{vdW} + U_{ele})$$

New: $f(\phi) = (\phi^2 - 1)^2$ , Old: $f(\phi) = (\phi - 1)^2$




Y. Zhao, Y. Ma, H. Sun, B. Li, and Q. Du, Comm Math Sci., accepted.

# Numerical Methods

# Exponential Time Differencing Scheme

$$\partial_t \phi = \gamma \left[ \epsilon \Delta \phi - \frac{1}{\epsilon} W'(\phi) \right] - f'(\phi)(\rho_w U_{vdW} + U_{ele})$$

$$\begin{aligned}
\partial_t \phi =& \mathcal{L}(\phi) + \mathcal{N}(\phi) \quad : \\
&\mathcal{L}(\phi) = \gamma(\epsilon \Delta \phi - \frac{\kappa}{\epsilon}\phi) - \mu\nu\phi \\
&\mathcal{N}(\phi) = -\frac{\gamma}{\epsilon}(W'(\phi) - \kappa\phi) - f'(\phi)(\rho_w U_{vdW} + U_{ele}) + \mu\nu\phi
\end{aligned}$$

$$\begin{aligned}
\kappa &\geq \frac{1}{2}\max\{0, \max_{0 \leq \phi \leq 1} W''(\phi)\} = 18 \\
\mu &\geq \frac{1}{2}\max\{0, \max_{0 \leq \phi \leq 1} f''(\phi)\} = 4 \\
\nu &= \sup_{x \in \Omega} |\rho_w U_{vdW} + U_{ele}|
\end{aligned}$$

# Spectral Spatial Discretization

$$\begin{aligned}\partial_t \hat{\phi}_{ijk} =& l_{ijk}\hat{\phi}_{ijk} + \widehat{\mathcal{N}(\Phi)}_{ijk}\\ l_{ijk} &= \gamma(\epsilon\lambda_{ijk} - \frac{\kappa}{\epsilon}) - \mu\nu\\ \lambda_{ijk} &= -\lambda_x^2 - \lambda_y^2 - \lambda_z^2\end{aligned}$$

$$\hat{\phi}_{ijk}(t_{n+1}) = e^{l_{ijk}\Delta t_n}\hat{\phi}_{ijk}(t_n) + e^{l_{ijk}\Delta t_n}\int_o^{\Delta t_n} e^{-l_{ijk}\tau}\left[\widehat{\mathcal{N}(\Phi)}(t_n+\tau)\right]_{ijk}\mathrm{d}\tau$$

# Runge-Kutta Approximation

- ETD1RK

$$\hat{\Phi}^{n+1} = ETD1RK(\hat{\Phi}^n, \Delta t_n, \mathcal{L}, \mathcal{N}) :$$
$$\phi_{ijk}^{n+1} = e^{l_{ijk}\Delta t_n}\hat{\phi}_{ijk}^{n} + l_{ijk}^{-1}(e^{l_{ijk}\Delta t_n} - 1)\left[\widehat{\mathcal{N}(\Phi^n)}\right]_{ijk}$$

- ETD2RK

$$\hat{\Phi}^{n+1} = ETD2RK(\hat{\Phi}^n, \Delta t_n, \mathcal{L}, \mathcal{N}) :$$
$$A = (a_{ijk}) = ETD1RK(\hat{\Phi}^n, \Delta t_n, \mathcal{L}, \mathcal{N}),$$
$$\phi_{ijk}^{n+1} = a_{ijk} + \Delta t_n^{-1} l_{ijk}^{-2}(e^{l_{ijk}\Delta t_n} - 1 - l_{ijk}\Delta t_n) \cdot \left[\widehat{\mathcal{N}(\check{A})} - \widehat{\mathcal{N}(\Phi^n)}\right]_{ijk}$$

- ETD4RK

# Numerical Results

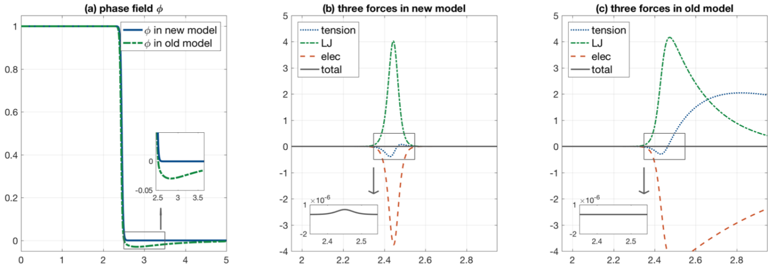
# One Particle System

$$F^{\epsilon,\mathrm{rad}}[\phi] = 4\pi\gamma_0 \int_0^\infty \left[\frac{\epsilon}{2}|\phi'(r)|^2 + \frac{1}{\epsilon}W(\phi(r))\right] r^2 \mathrm{d}r$$
$$+ 4\pi\rho_w \int_0^\infty f(\phi)U_{vdW}(r)r^2\mathrm{d}r + \frac{Q^2}{8\pi\epsilon_0}\left(\frac{1}{\epsilon_w} - \frac{1}{\epsilon_m}\right)\int_0^\infty f(\phi)/r^2\mathrm{d}r$$

| | |
|---|---|
| $P = 0\ pN/\text{Å}^2$ | Pressure |
| $T = 300$ K | Tempature |
| $\gamma_0 = 0.175\ k_\mathrm{B}T/\text{Å}^2$ | Surface tension |
| $\rho_\mathrm{w} = 0.0333\ \text{Å}^{-3}$ | The constant solvent (water) density |
| $\varepsilon_i = \varepsilon_\mathrm{LJ} = 0.3\ k_\mathrm{B}T,\ \ i = 1:N$ | The depth of the Lennard-Jones potential well associated with the $i$th solute atom |
| $\sigma_i = \sigma_\mathrm{LJ} = 3.5$ Å, $\ i = 1:N$ | The finite distance at which the Lennard-Jones potential of $i$th solute atom is zero |
| $r_\mathrm{cut} = 0.7\sigma_\mathrm{LJ}$ | The radius of truncation for potential |
| $\varepsilon_0 = 1.4321 \times 10^{-4}\ \mathrm{e}^2/(k_\mathrm{B}T\text{Å})$ | Vacuum permittivity |
| $\varepsilon_\mathrm{m} = 1$ | Relative permittivity of the solute |
| $\varepsilon_\mathrm{w} = 80$ | Relative permittivity of the solvent (water) |
| $Q_i$ in units e | Partial charge of the $i$th solute atom at $\mathbf{x}_i$ which may vary in different examples |
| $\epsilon$ in units Å | The interfacial width of the phase field $\phi$, which vary in different examples |

$$\partial_t \phi = -\delta F^{\epsilon,\mathrm{rad}}[\phi]/\delta\phi \qquad \text{with} \quad Q = 2e \text{ and } \epsilon = 0.1\mathring{A}$$

New: $f(\phi) = (\phi^2 - 1)^2$ , Old: $f(\phi) = (\phi - 1)^2$

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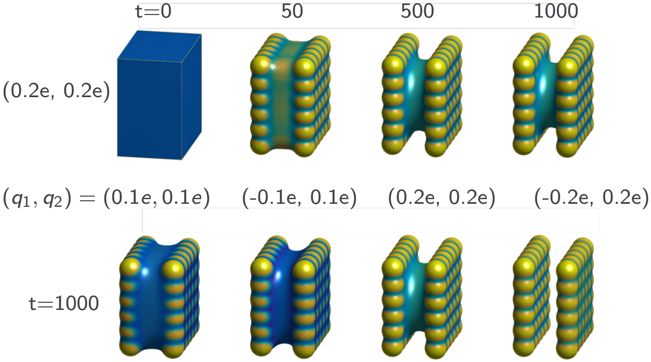
# One Particle System

$$F[\Gamma] := F(R) = 4\pi\gamma_0 R^2 + 16\pi\rho_w\epsilon\left(\frac{\sigma^{12}}{9R^9} - \frac{\sigma^6}{3R^3}\right) + \frac{Q^2}{8\pi\epsilon_0 R}\left(\frac{1}{\epsilon_w} - \frac{1}{\epsilon_m}\right)$$

| $Q$ | Optimal Radii/Energy | $\epsilon = 0.5$ | $\epsilon = 0.2$ | $\epsilon = 0.05$ | $\epsilon = 0.02$ | $\epsilon = 0$ |
|---|---|---|---|---|---|---|
| 0.0 | $R_{\text{min}}$ | 3.080 | 3.060 | 3.055 | 3.054 | 3.054 |
| | $F_{\text{surf}}$ | 20.904 | 20.603 | 20.514 | 20.510 | 20.511 |
| | $F_{\text{vdW}}$ | -2.558 | -2.614 | -2.627 | -2.638 | -2.644 |
| | $F_{\text{elec}}$ | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| | $F_{\text{tot}}$ | 18.346 | 17.990 | 17.887 | 17.872 | 17.867 |
| 0.5 | $R_{\text{min}}$ | 2.987 | 2.967 | 2.961 | 2.960 | 2.960 |
| | $F_{\text{surf}}$ | 19.672 | 19.366 | 19.275 | 19.266 | 19.267 |
| | $F_{\text{vdW}}$ | -0.980 | -1.025 | -1.036 | -1.042 | -1.054 |
| | $F_{\text{elec}}$ | -23.080 | -23.162 | -23.177 | -23.177 | -23.173 |
| | $F_{\text{tot}}$ | -4.388 | -4.822 | -4.938 | -4.953 | -4.960 |
| 1.0 | $R_{\text{min}}$ | 2.798 | 2.779 | 2.773 | 2.772 | 2.771 |
| | $F_{\text{surf}}$ | 17.325 | 16.994 | 16.904 | 16.890 | 16.886 |
| | $F_{\text{vdW}}$ | 5.104 | 5.112 | 5.115 | 5.115 | 5.115 |
| | $F_{\text{elec}}$ | -98.542 | -98.923 | -99.006 | -99.011 | -99.012 |
| | $F_{\text{tot}}$ | -76.113 | -76.817 | -76.99 | -77.006 | -77.012 |
| 1.5 | $R_{\text{min}}$ | 2.617 | 2.601 | 2.594 | 2.593 | 2.593 |
| | $F_{\text{surf}}$ | 15.315 | 14.891 | 14.800 | 14.786 | 14.782 |
| | $F_{\text{vdW}}$ | 17.837 | 17.950 | 17.970 | 17.972 | 17.971 |
| | $F_{\text{elec}}$ | -236.989 | -237.869 | -238.087 | -238.101 | -238.105 |
| | $F_{\text{tot}}$ | -203.836 | -205.028 | -205.318 | -205.343 | -205.354 |
| 2.0 | $R_{\text{min}}$ | 2.468 | 2.456 | 2.449 | 2.449 | 2.448 |
| | $F_{\text{surf}}$ | 13.941 | 13.304 | 13.194 | 13.183 | 13.178 |
| | $F_{\text{vdW}}$ | 38.471 | 38.676 | 38.764 | 38.758 | 38.757 |
| | $F_{\text{elec}}$ | -446.416 | -447.827 | -448.280 | -448.306 | -448.317 |
| | $F_{\text{tot}}$ | -394.004 | -395.848 | -396.322 | -396.365 | -396.381 |

# Two Plates System

- Each plate consists of $6 \times 6$ fixed $\mathrm{CH}_2$ atoms; inter-atom distance $d_0 = 4.389\AA$; plate-plate distance $d = 12\AA$

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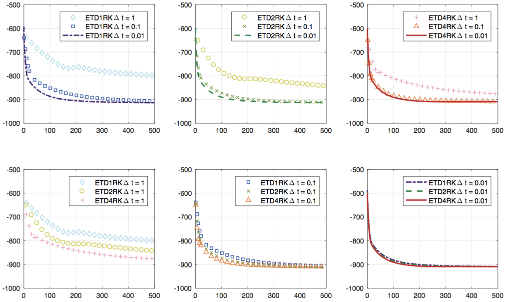
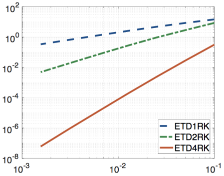
# Two Plates System

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# Future Work

$$-\nabla\cdot\epsilon(\phi)\nabla\psi_\phi + f(\phi)V'(\psi_\phi) = \rho_f$$

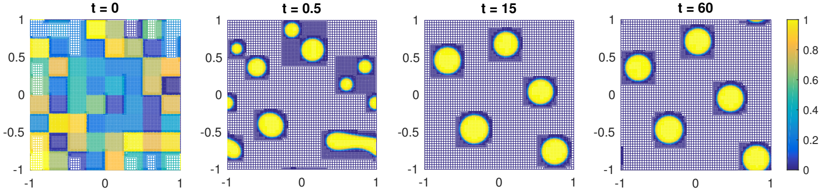
$$V(\psi_\phi) = \begin{cases} \beta^{-1}\sum_{j=1}^{M} c_j^\infty\left(e^{-\beta q_j\psi_\phi}-1\right) & \text{for nonlinear PB} \\ \frac{1}{2}\epsilon_w\epsilon_0\kappa^2\psi_\phi^2 & \text{for linearized PB} \end{cases}$$

$$\partial_t\phi = \gamma\left[\epsilon\Delta\phi - \frac{1}{\epsilon}W'(\phi)\right] - \rho_w f'(\phi)U_{vdW} + \frac{\epsilon'(\phi)}{2}|\Delta\phi|^2 + f'(\phi)V(\psi)$$

$$-\nabla\cdot\epsilon(\phi)\nabla\psi_{reac} + f(\phi)V'(\psi_{reac}+\psi_{vac}) = \nabla\cdot\left[\epsilon(\phi)-\epsilon_m\epsilon_0\right]\nabla\psi_{vac}$$

# Adaptive Mesh Refinement

**for** *i from 1 to maximum number of levels* **do**
  **for** *each patch at level i* **do**
    Tag all the grid points where $|\nabla\phi|$ is above a threshold;
    Use Berger-Rigoutsos algorithm to find sub-patches containing the tagged points;
    **if** *sub-patches are not well-nested* **then**
      recursively add a layer of points correspondingly to enforce well-nestedness;
    **end**
    Add sub-patches to level the patch list at level $i+1$;
  **end**
**end**



# Acknowledgement

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Prof. Bo Li, University of California, San Diego
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# Q & A

Thank you!