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DEGAUSS: A Revolutionary Softcore Force Field for Molecular Dynamics Simulations

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The Problem: Classical Force Fields Have Fatal Singularities

Classical molecular dynamics force fields contain mathematical singularities that cause numerical failures in alchemical free energy calculations and inaccurate descriptions in short-range interactions.

Lennard-Jones Potential: $V_{\text{LJ}}(r_{ij}) = 4\epsilon_0 \left[\left(\frac{r_m}{r_{ij}}\right)^{12} - \left(\frac{r_m}{r_{ij}}\right)^{6} \right] \xrightarrow{r \to 0} \infty$

Coulomb Potential: $V_{\text{Coulomb}}(r_{ij}) = \frac{1}{4\pi\epsilon_0}\frac{q_i q_j}{r_{ij}} \xrightarrow{r \to 0} \infty$

Consequences of Singularities:

- Simulation crashes during particle creation/annihilation in alchemical free energy calculations
- Exclusion of 1-2, 1-3 terms that distort physics
- Missing charge penetration effects
- Inaccurate short-range interactions, leading to insufficient (too repulsive or too attractive) behavior

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The DEGAUSS Solution: Two Revolutionary Components

DEGAUSS eliminates singularities through two mathematically elegant potential functions that maintain classical accuracy while providing finite energies at all distances.

Double Exponential Van der Waals Potential:

$$V_{\text{DE}}(r) = \epsilon_0 \left(\frac{\beta e^{\alpha}}{\alpha - \beta} e^{-\alpha r / r_m} - \frac{\alpha e^{\beta}}{\alpha - \beta} e^{-\beta r / r_m} \right)$$

Key Features: Finite energy at $r = 0$, reproduces Lennard-Jones behavior at normal distances. Parameters α and β control the repulsive and attractive steepness, allowing tunable softness.

Gaussian Charge Electrostatics:

$$V_{\text{Gauss}}(r_{ij}) = \frac{q_i q_j}{r_{ij}} \text{erf}(\beta_{ij} r_{ij})$$

Key Features: Natural charge penetration effects, $V(0) = 0$, smooth transition to Coulombic behavior. Gaussian radius $1/\beta$ controls the extent of charge distribution and softness.

DEGAUSS Advantages:

- No singularities - finite energies at all distances
- Physical accuracy - maintains classical force field behavior
- Minimal reparameterization - preserves existing force field parameters

Electrostatic Foundation: pGM polarizable force field

General pGM Formulation: The charge density for an atom with multipole moments is given by: $\rho(\vec{r}; \vec{R}) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} \frac{(-1)^l q_{lm}}{l!} \left(\frac{\beta}{\sqrt{\pi}}\right)^3 \beta^{2l} \nabla^l Y_l^m(\hat{r}) \exp(-\beta^2 |\vec{r} - \vec{R}|^2)$

DEGAUSS Uses the Monopole Term (l=0): $\rho(\vec{r}; \vec{R}) = q \left(\frac{\beta}{\sqrt{\pi}}\right)^3 \exp(-\beta^2 |\vec{r} - \vec{R}|^2)$

The pGM framework has been extensively validated for achieving near-quantum mechanical accuracy in electrostatic interactions while maintaining computational efficiency.

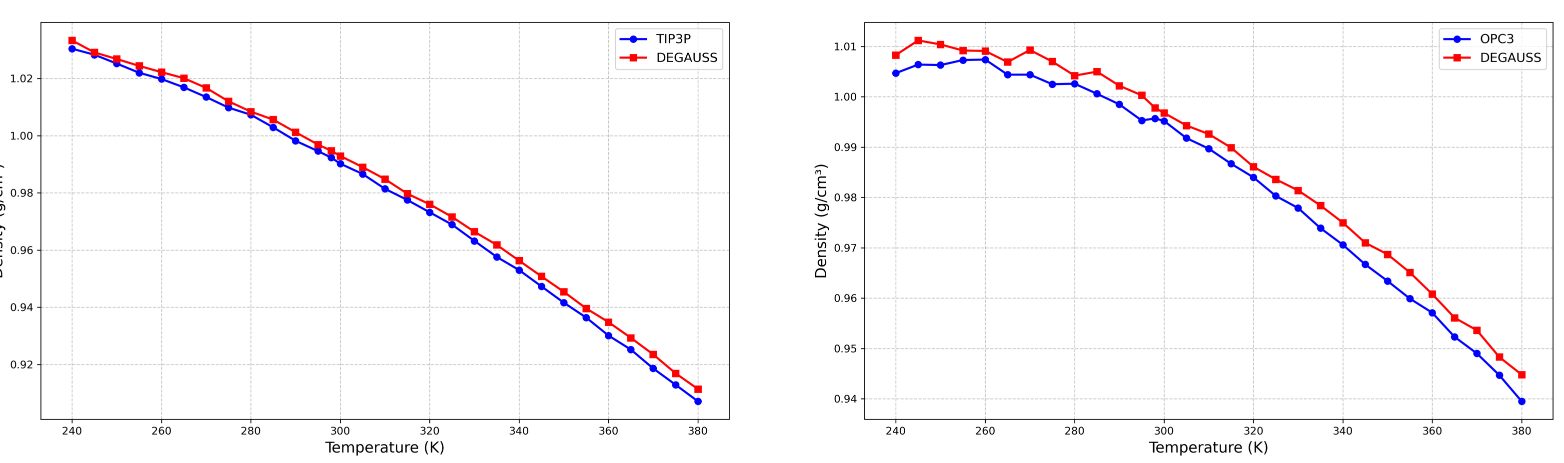
Comprehensive Validation: DEGAUSS Maintains Classical Accuracy

Extensive validation across water models, peptides, and proteins demonstrates that DEGAUSS accurately reproduces classical force field behavior while eliminating singularities.

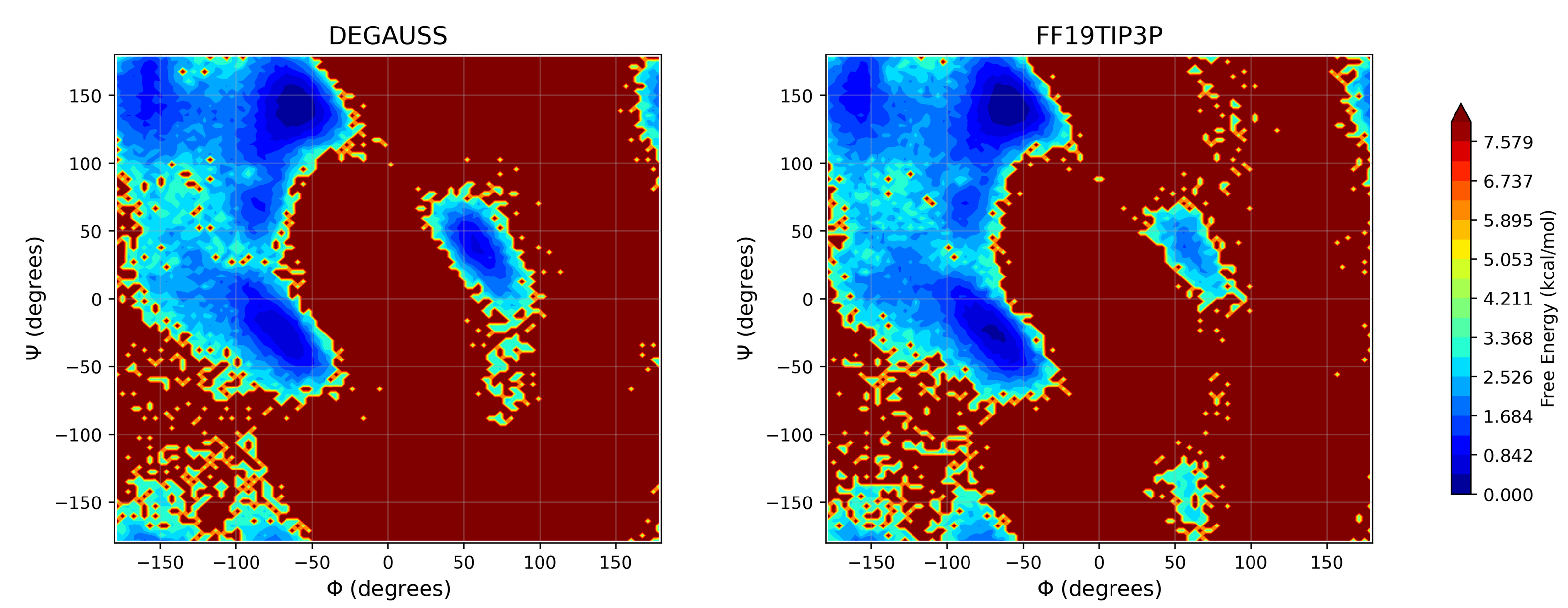
Water Model Validation - Thermodynamic Properties:

Property	Experimental	TIP3P	TIP3P-DEGAUSS	OPC3	OPC3-DEGAUSS
ρ [g/cm^3]	0.997	0.992	0.994	0.996	0.998
ε_0	78.4	98.33	97.59	71.33	77.57
D [10^9 m^2/s]	2.30	5.21	4.57	2.44	2.18
ΔH_{vap} [kcal/mol]	10.52	9.90	9.94	11.74	11.80
κ_T [10^{-6} bar^{-1}]	45.9	57.35	55.02	44.94	47.06

Temperature-Dependent Behavior:



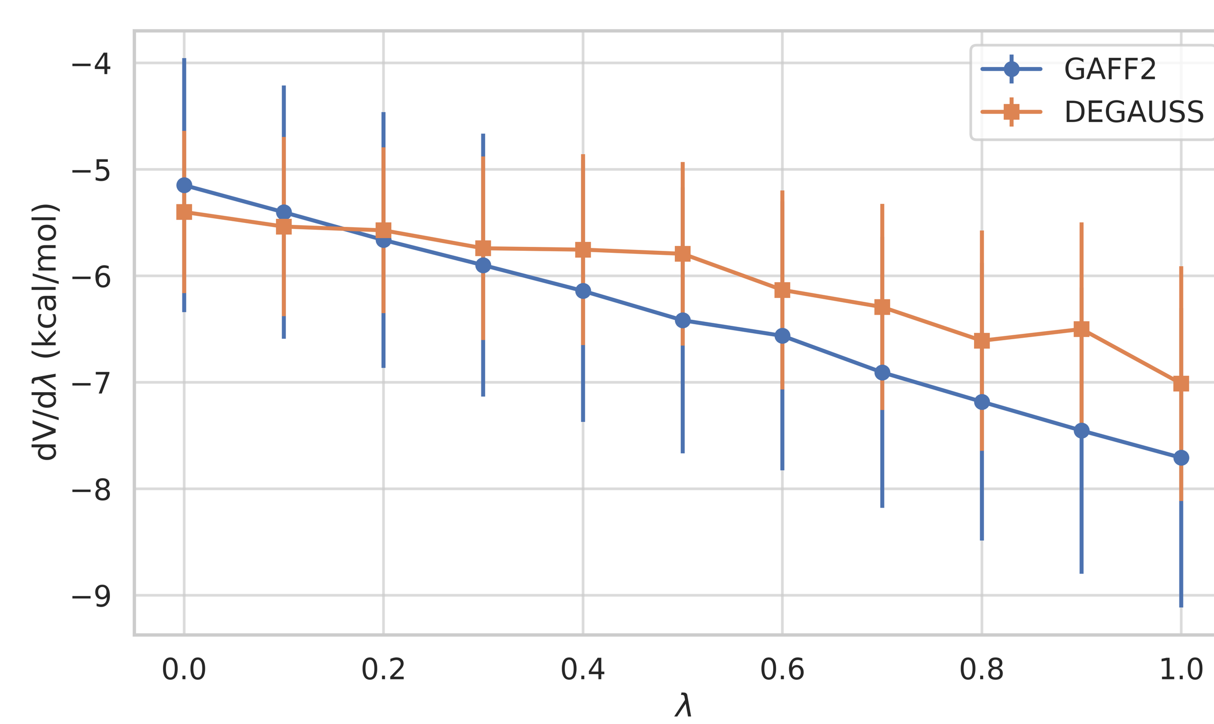
Conformational Sampling - Alanine Dipeptide:



Enhanced Alchemical Free Energy Calculations

DEGAUSS demonstrates superior numerical stability in alchemical transformations without requiring additional softcore potentials or reparameterization.

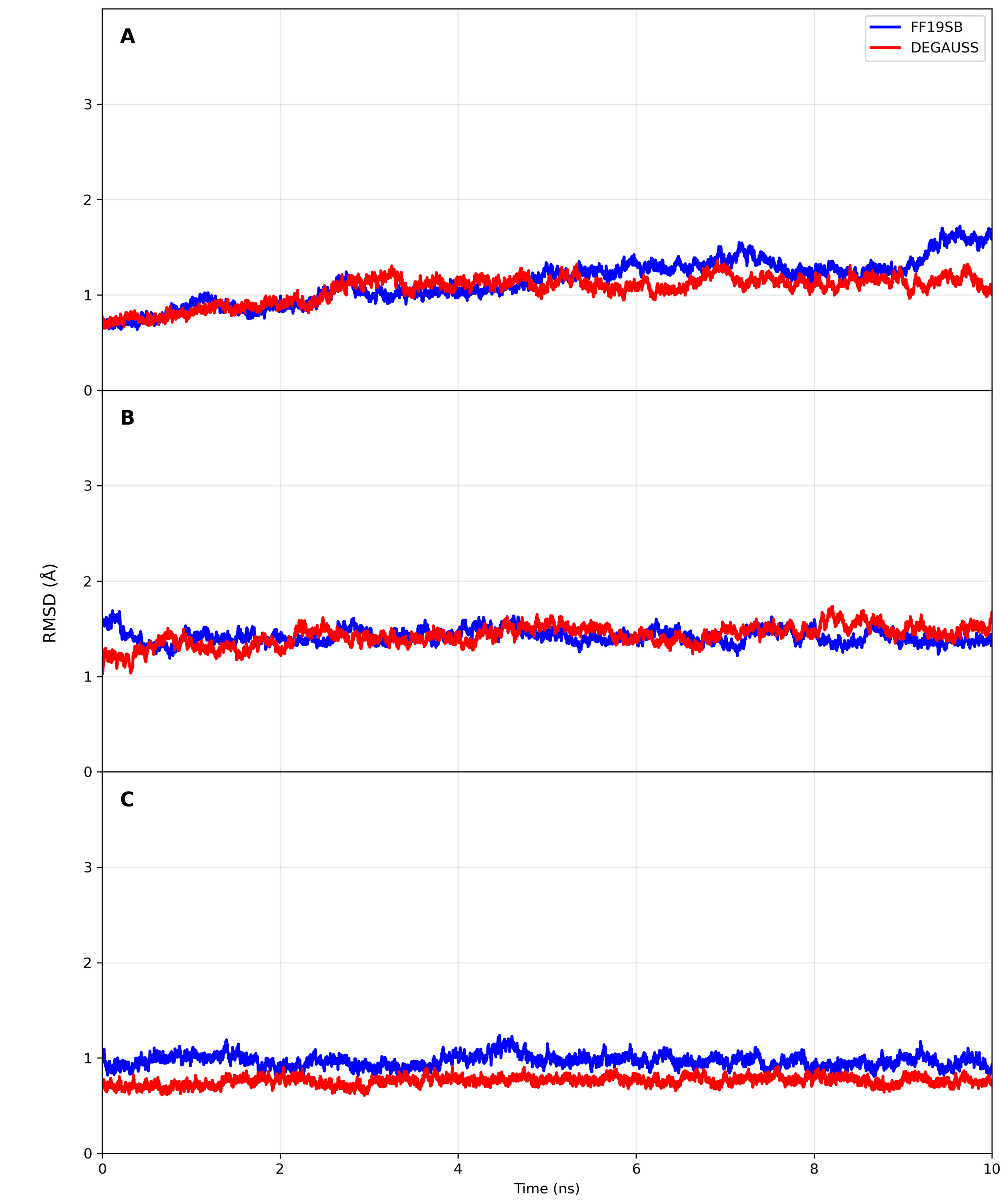
Benzene → Phenol Transformation (Decharging Step):



Key Advantages:

- Reduced statistical noise - 29% smaller standard deviations
- No reparameterization needed - uses identical GAFF2 parameters
- No additional softcore potentials - inherently smooth

Protein Structural Stability:

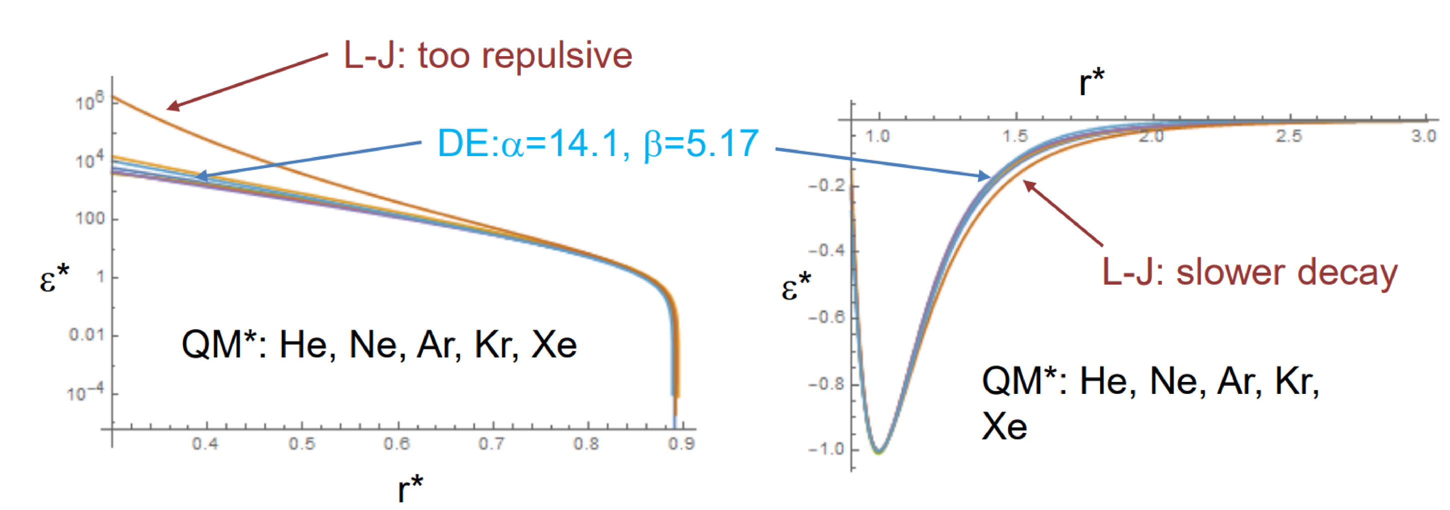


Complete Benzene → Phenol Transformation Results:

Transformation Step	Force Field	ΔG (kcal/mol)	Average Std Dev
2*Decharging	GAFF2	-6.42	1.25
	GAFF2-DEGAUSS	-5.99	**0.89**
2*Van der Waals	GAFF2	1.34	0.85
	GAFF2-DEGAUSS	1.19	**0.62**
2*Recharging	GAFF2	-33.71	1.45
	GAFF2-DEGAUSS	-33.16	**1.08**
2*Total ΔG	GAFF2	$\mathbf{-38.79}$	**1.18**
	GAFF2-DEGAUSS	$\mathbf{-37.96}$	**0.86**
Overall Improvement		Comparable accuracy	27% reduction

Flexible Control for quantum level accuracy

The control parameters α and β in DE potential and Gaussian radii in electrostatics can be systematically tuned to match high-level quantum mechanical calculations, enabling accurate reproduction of diverse interaction profiles across different chemical systems.



Future Work

DEGAUSS water model incorporating O-H interactions in van der Waals terms to build a new water model where all parameters are derived from high-level quantum mechanical data.