Hylleraas

Automated Determination of Hybrid Particle-Field Parameters by Machine Learning

May 29, 2020

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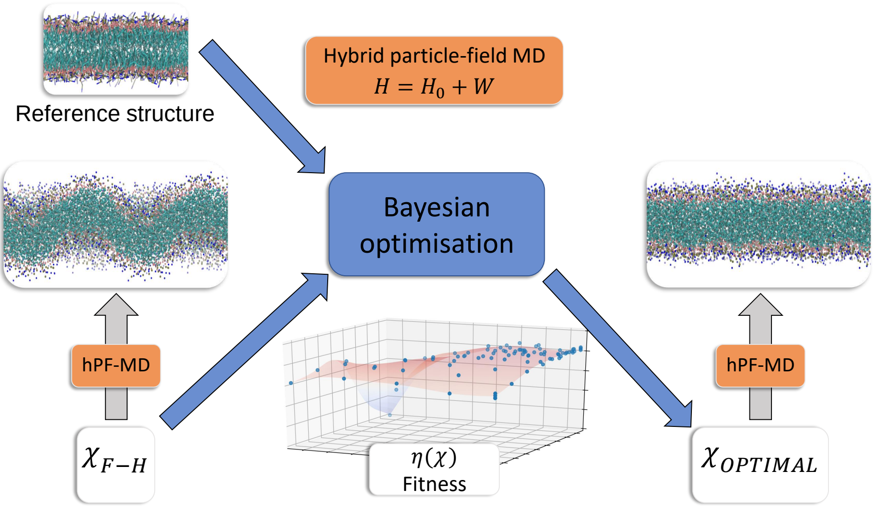
Norwegian Centre of Excellence

The Research Council of Norway

UiO : University of Oslo

Outline



Reference structure
Hybrid particle-field MD
$H = H_0 + W$
Bayesian optimisation
hPF-MD
χ_{F-H}
$\eta(\chi)$
Fitness
hPF-MD
$\chi_{OPTIMAL}$

Outline

Introduction
- Hybrid particle-field (hPF)
- Coarse-graining

Bayesian optimization
- Gaussian process
- Acquisition function

Lipid membranes
- Feature importance
- Transferability

Summary

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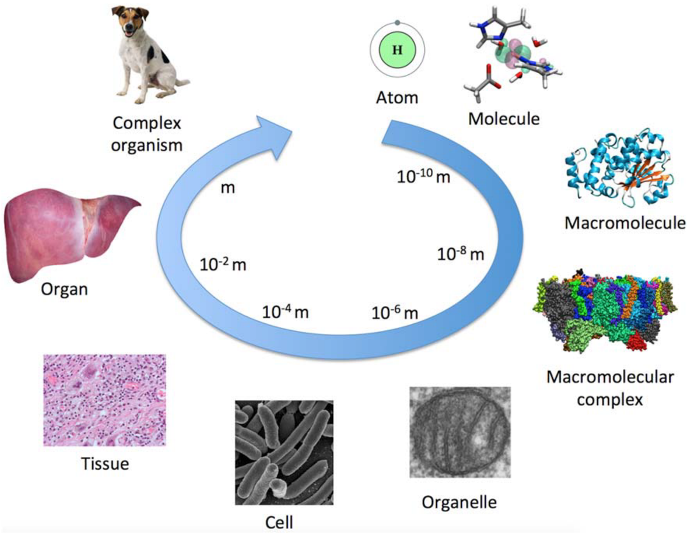
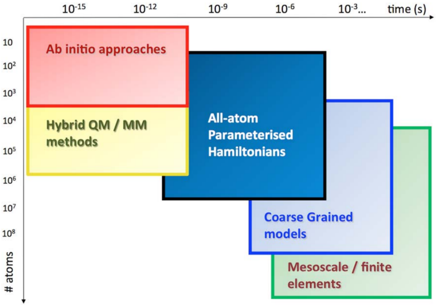
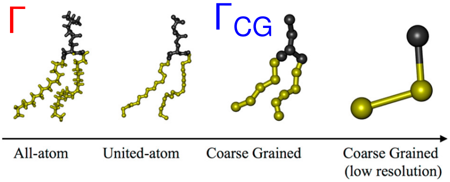


M. Cascella and S. Vanni, Chem. Modell. ***12****, 1–52 (2016)*

Coarse-graining





$$Z = \int \mathrm{d}\Gamma \; e^{-\beta H(\Gamma)} \quad \longrightarrow \quad Z \simeq \int \mathrm{d}\Gamma_{\mathrm{CG}} \; e^{-\beta H(\Gamma_{\mathrm{CG}})}$$

M. Cascella and S. Vanni, Chem. Modell. ***12***, *1–52 (2016)*
T.A. Soares et al., J. Phys. Chem. Lett. ***8***, *3586–3594 (2017)*

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Hybrid particle-field

Hamiltonian

$$H(\{\mathbf{r}\}) = \sum_{m=1}^{N_{\text{mol}}} \underbrace{H_0(\{\mathbf{r}_m\})}_{\text{Intramolecular}} + \underbrace{W[\{\phi(\mathbf{r})\}]}_{\text{Intermolecular}}$$

External potential and forces

$$V_k(\mathbf{r}) = \frac{\delta W[\{\phi\}]}{\delta \phi_k(\mathbf{r})}, \quad \textit{and} \quad \mathbf{F}_i = -\nabla_i V_k(\mathbf{r}_i)$$

Interaction energy $W[\{\phi(\mathbf{r})\}]$

$$W\left[\phi(\mathbf{r})\right] = \frac{1}{2\phi_0}\int \mathrm{d}\mathbf{r} \left(\underbrace{\sum_{ij} \tilde{\chi}_{ij}\phi_i(\mathbf{r})\phi_j(\mathbf{r})}_{\textit{Mixing}} + \underbrace{\frac{1}{\kappa}\left(\sum_j \phi_j(\mathbf{r}) - \phi_0\right)^2}_{\textit{Compressibility}} \right),$$

Depends on a set of parameters

$\tilde{\chi}_{ij} < 0$ Particle types i and j prefer to mix

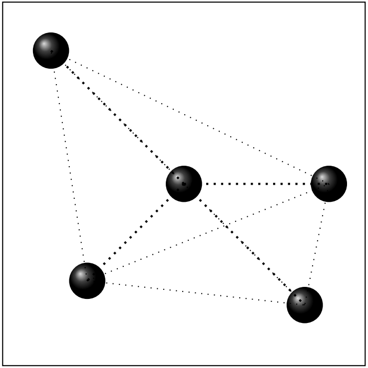
$\tilde{\chi}_{ij} > 0$ Particle types i and j prefer to avoid each other

and

$\kappa = 0$ Incompressible

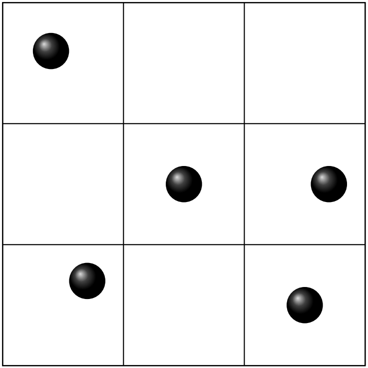
$\kappa \gg 0$ Compressible

Computing the density field



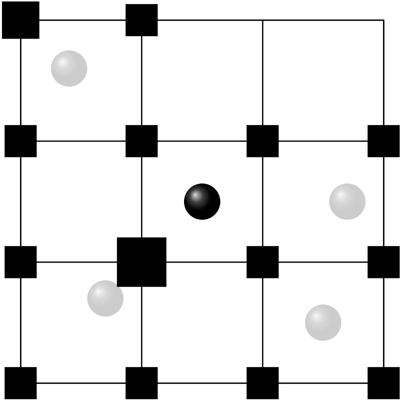
$$\sum_{ij} \tilde{V}(\mathbf{r}_{ij})$$

Computing the density field



$$\sum_i V_k[\phi(\mathbf{r}_i)]$$

Computing the density field

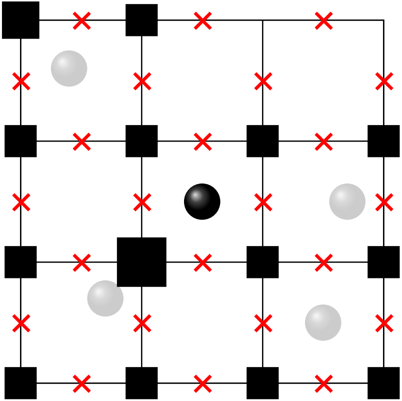


$$\sum_i V_k[\phi(\mathbf{r}_i)]$$

$$\mathbf{F}_i = -\nabla_i V_k[\phi(\mathbf{r}_i)]$$

$\blacksquare$: ϕ_{nml}

Computing the density field



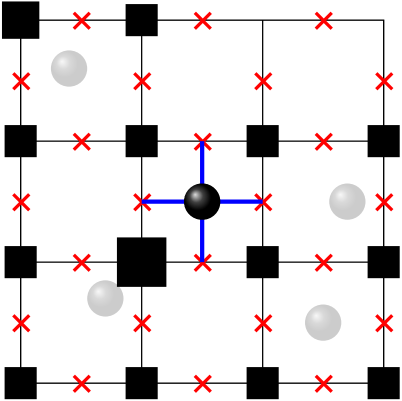
$$\sum_i V_k[\phi(\mathbf{r}_i)]$$

$$\mathbf{F}_i = -\nabla_i V_k[\phi(\mathbf{r}_i)]$$

■ : ϕ_{nml}

✕ : ∇V_{nml}

Computing the density field



$$\sum_i V_k[\phi(\mathbf{r}_i)]$$

$$\mathbf{F}_i = -\nabla_i V_k[\phi(\mathbf{r}_i)]$$

■ : ϕ_{nml}

✕ : ∇V_{nml}

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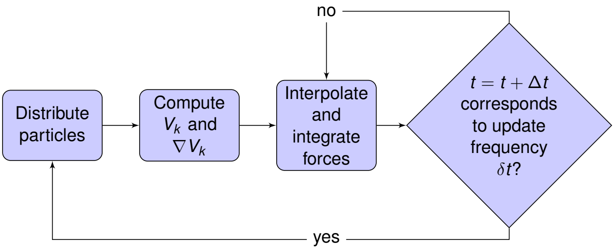
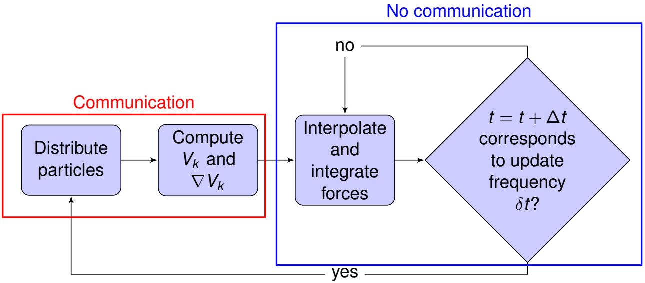
Implementation

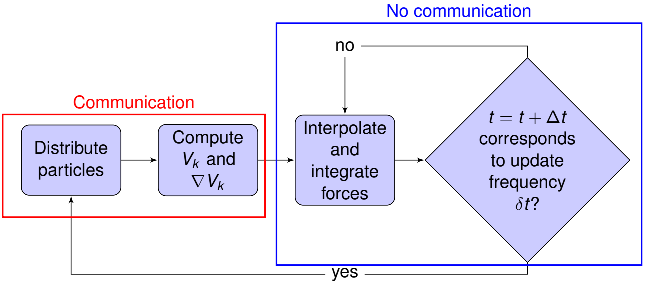


Implementation

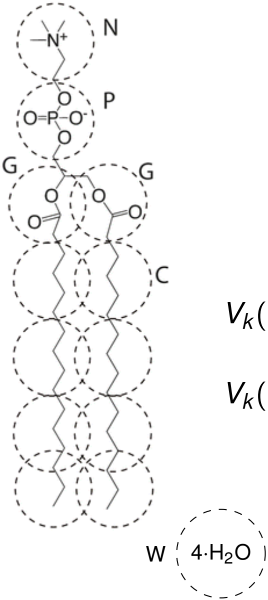


Implementation

OCCAM
Molecular Dynamics



Coarse grained model



Intramolecular Hamiltonian

$$H_0 = \sum \frac{m_i \dot{\mathbf{r}}_i^2}{2} + \sum \frac{k_r (r_{ij} - r_0)^2}{2} + \sum \frac{k_\theta (\cos(\theta_{ijk}) - \cos(\theta_0))^2}{2}$$

Interaction potential

$$V_k(\mathbf{r}) = \frac{\delta W[\{\phi\}]}{\delta \phi_k(\mathbf{r})}$$

$$V_k(\mathbf{r}) = \frac{1}{\phi_0} \left(\sum \tilde{\chi}_{ij} \phi_j(\mathbf{r}) + \frac{1}{\kappa} \left(\sum \phi_j(\mathbf{r}) - \phi_0 \right) \right)$$

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Flory-Huggins $\tilde{\chi}$ matrix

P	G	C	D	W	
-1.5	6.3	9.0	7.2	-8.1	N
	4.5	13.5	11.7	-3.6	P
		6.3	6.3	4.5	G
			0	13.5	C
				23.25	D

Calculated from

$$\chi^{\text{F–H}}_{KK'} = \frac{z_{\text{CN}}}{2k_{\text{B}}T}\left[\frac{2u_{KK'} - (u_{KK} + u_{K'K'})}{2}\right],$$

where $u_{KK'}$ is interpreted as the MARTINI model K–K' ε parameter.

Bayesian optimization

Constrained optimization scheme

$$\mathbf{x}_{\text{optimal}} = \arg\max_{\mathbf{x} \in \mathcal{X}} \eta(\mathbf{x})$$

Does not require derivatives, suitable for computationally expensive, noisy black-box functions.

Parameters $\mathbf{x} = (p_1, p_2, \ldots, p_n)$

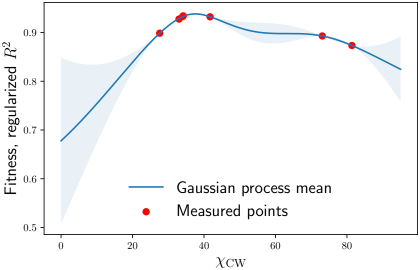
Parameter space $\mathcal{X}$

Objective function $\eta(\mathbf{x})$

Surrogate-based optimization

In general the parameter space $\mathcal{X}$ is high-dimensional and the objective function $\eta(\mathbf{x})$ is unknown, non-convex, multimodal, and only accessible through noisy pointwise sampling.

$\rightarrow$ Place a **Gaussian process** function *prior* over the objective function and optimize it instead.



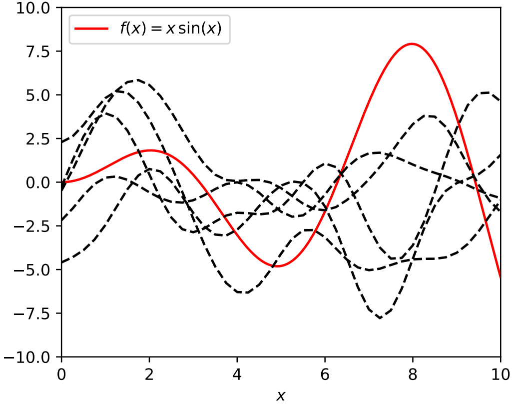
Gaussian process

A GP is a collection of random variables such that any linear combination of the variables induces a multivariate normal distribution.

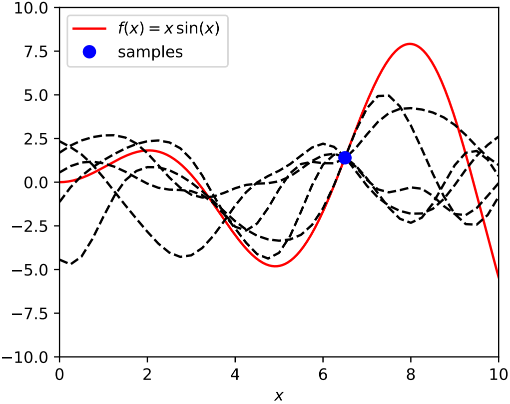
Given data, a GP is a probability distribution over possible functions which fits the data points.

$$f(x) \sim \mathcal{GP}(\mu_0, \Sigma_0)$$

Conditioning



Conditioning



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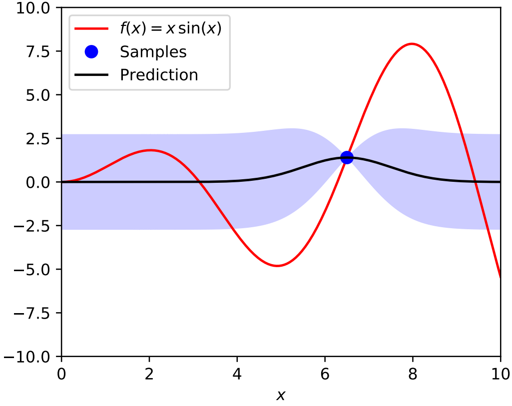
Conditioning



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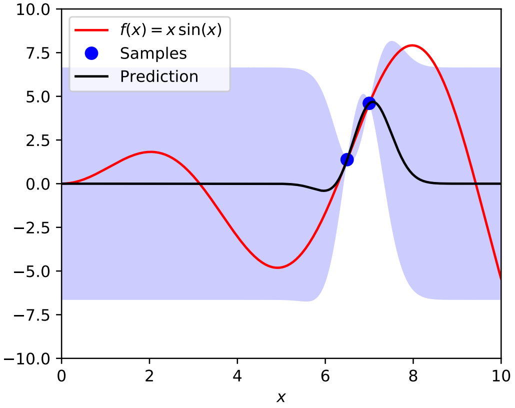
Conditioning



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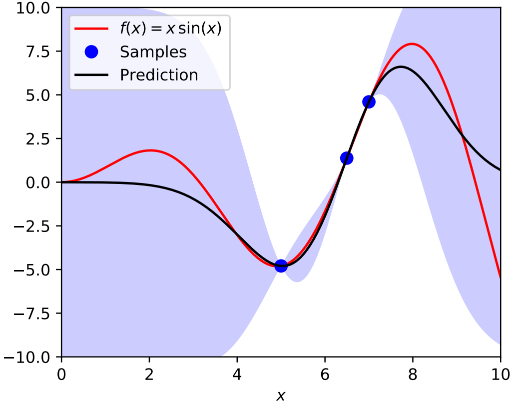
Conditioning



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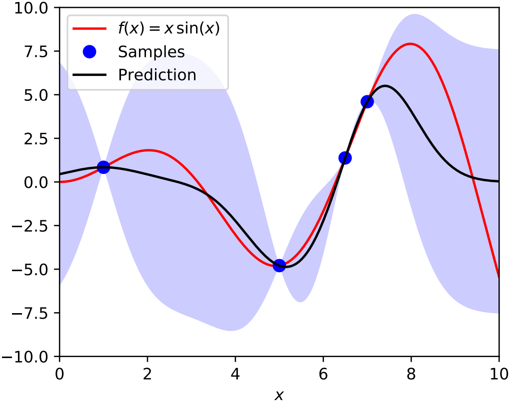
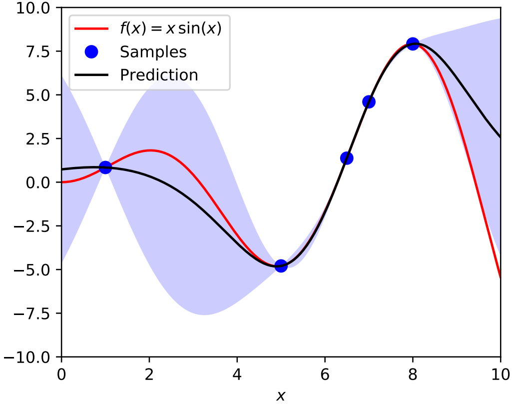
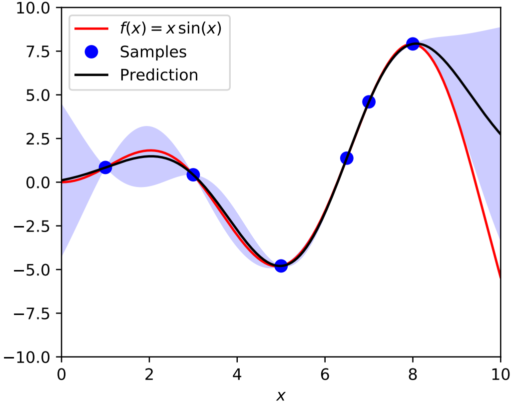
Conditioning



Conditioning



Conditioning



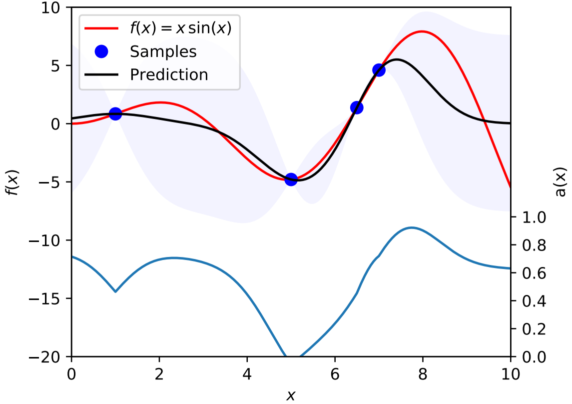
Acquisition function

In order to turn the GP into an optimization scheme, we pair it with an **acquisition function** to guide the sampling

$$\begin{aligned} a(\mathbf{x}) &= a(\mu(\mathbf{x}), \sigma(\mathbf{x})) \\ &= \mu(\mathbf{x}) + \beta\sigma(\mathbf{x}) \end{aligned}$$

Acquisition function

$\beta = 1.0$



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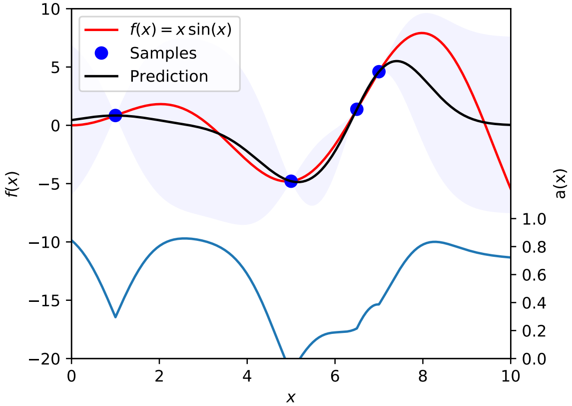
Acquisition function

$\beta = 3.0$



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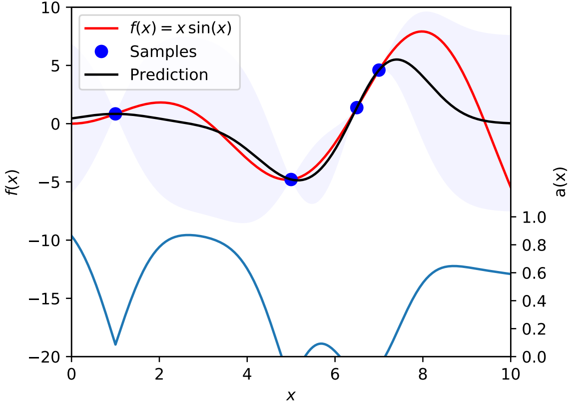
Acquisition function

$\beta = 5.0$



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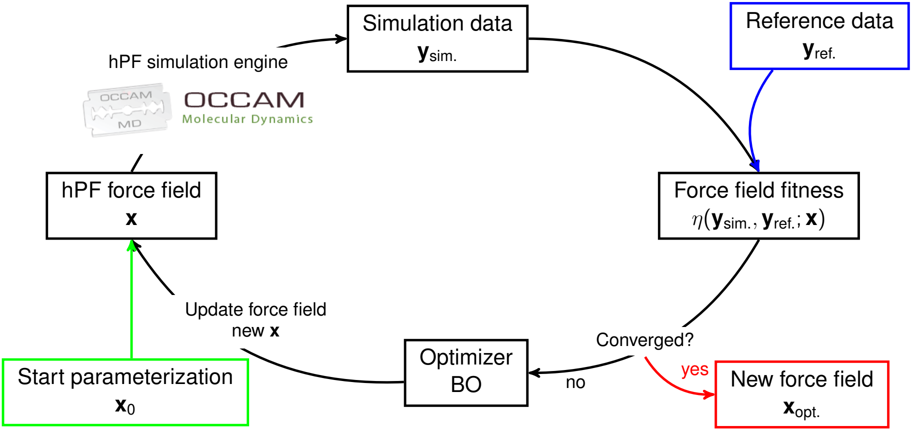
Bayesian optimization



Introduction

Bayesian optimization

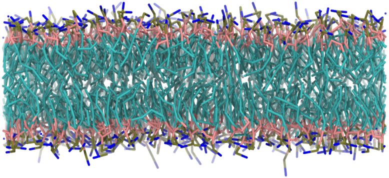
Lipid membranes

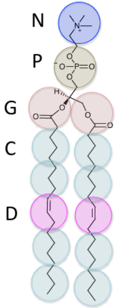
- Feature importance
- Transferability

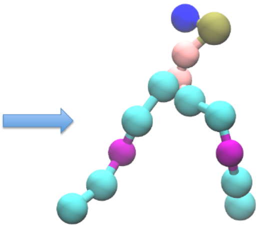
Summary

Lipid membrane test systems

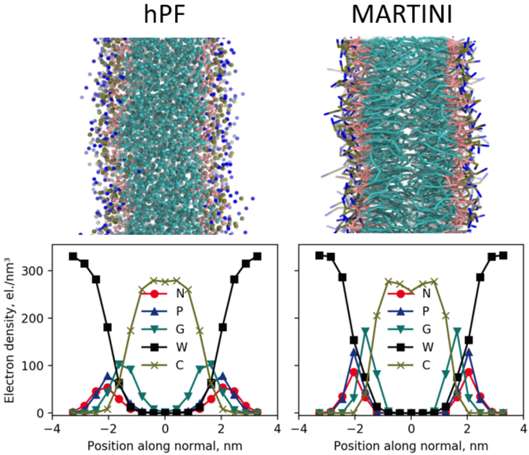
Dipalmitoylphosphatidylcholine (DPPC)
Dimyristoylphosphatidylcholine (DMPC)
Distearoylphosphatidylcholine (DSPC)
Dioleoylphosphatidylcholine (DOPC)





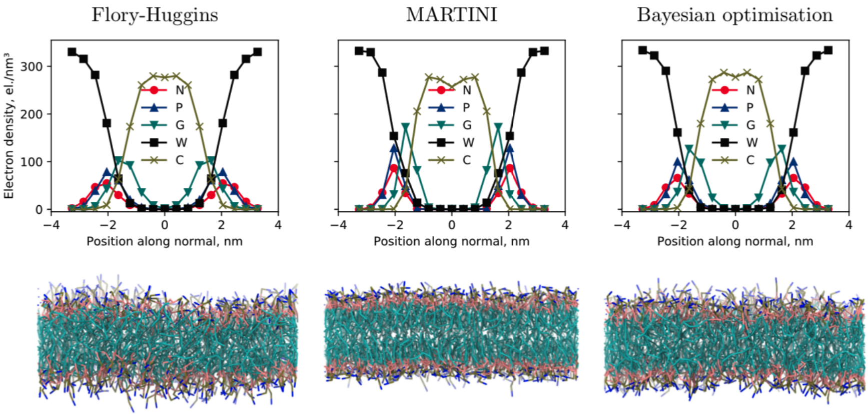


Fitness function



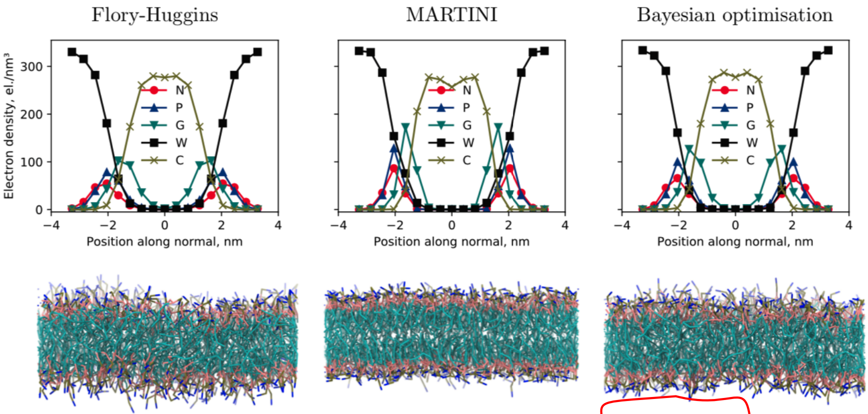
$$\eta(\varphi;\tilde{\chi}) = \frac{1}{nn_k}\sum_{k=1}^{n_k}\sum_{i=1}^{n}\left|\varphi_i^k - \hat{\varphi}_i^k\right|^2,$$

Optimized DPPC parameters



	N	P	G	C	W	average
BO (this work)	4.65	4.10	6.52	7.26	8.91	6.29 (1.71%)
F-H [21]	9.29	12.19	20.51	12.23	12.82	13.41 (4.10%)

Optimized DPPC parameters



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F-H [21]	9.29	12.19	20.51	12.23	12.82	13.41 (4.10%)

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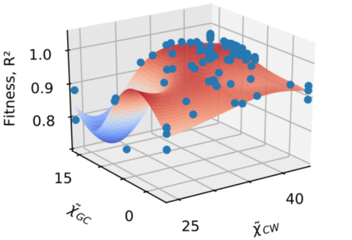
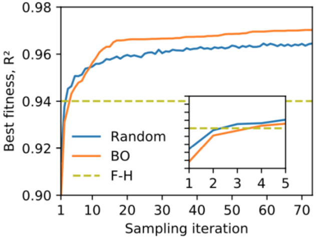
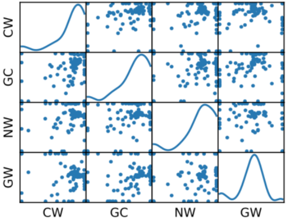
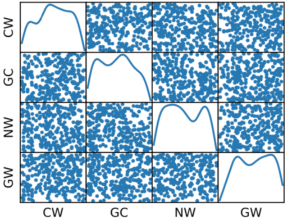
Sampling efficiency







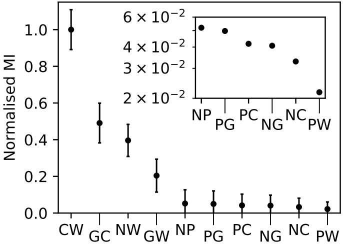
Bayesian optimization sampling

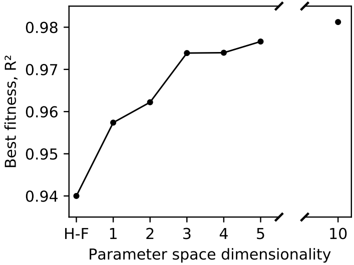


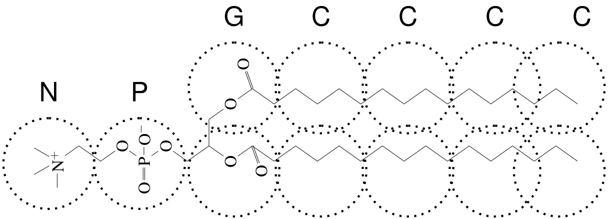
Random sampling

Feature importance

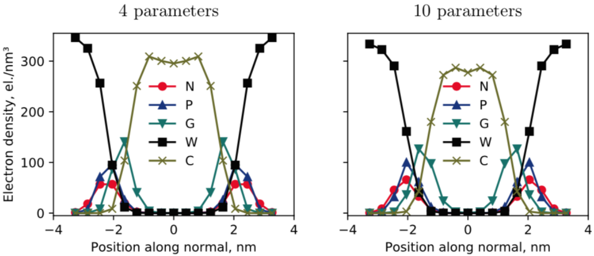
$$MI(X;Y) = -\int_{\mathcal{X}}\int_{\mathcal{Y}} \mathrm{d}x\mathrm{d}y\, f_{X,Y}(x,y)\log\frac{f_{X,Y}(x,y)}{f_X(x)f_Y(x)},$$





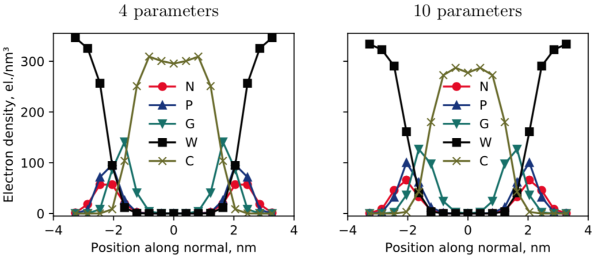


Feature importance



	parameter space dimensionality				
	10	4	3	2	1
C–W	42.24	43.68	43.63	42.09	38.16
G–C	10.47	14.00	15.33	14.69	6.30
N–W	-3.77	1.55	1.82	-8.10	-8.10
G–W	4.53	3.02	4.50	4.50	4.50
N–P	-9.34	-1.50	-1.50	-1.50	-1.50
P–G	8.04	4.50	4.50	4.50	4.50
N–G	1.97	6.30	6.30	6.30	6.30
P–C	14.72	13.50	13.50	13.50	13.50
P–W	-1.51	-3.60	-3.60	-3.60	-3.60
N–C	13.56	9.00	9.00	9.00	9.00
S_{p}	1.71%	1.96%	2.25%	2.29%	2.32%

Feature importance



	parameter space dimensionality				
	10	4	3	2	1
C–W	42.24	43.68	43.63	42.09	38.16
G–C	10.47	14.00	15.33	14.69	6.30
N–W	-3.77	1.55	1.82	-8.10	-8.10
G–W	4.53	3.02	4.50	4.50	4.50
N–P	-9.34	-1.50	-1.50	-1.50	-1.50
P–G	8.04	4.50	4.50	4.50	4.50
N–G	1.97	6.30	6.30	6.30	6.30
P–C	14.72	13.50	13.50	13.50	13.50
P–W	-1.51	-3.60	-3.60	-3.60	-3.60
N–C	13.56	9.00	9.00	9.00	9.00
S_p	1.71%	1.96%	2.25%	2.29%	2.32%

Transferability

	DPPC					
	N	P	G	C	W	average
DPPC-optimised	4.65	4.10	6.52	7.26	8.91	6.29 (1.71%)
DMPC-optimised	4.45	4.05	6.44	8.37	8.36	6.34 (1.97%)
DOPC-optimised	5.39	8.15	12.05	9.81	6.51	8.38 (2.61%)
DSPC-optimised	5.02	6.08	8.71	9.40	9.63	7.76 (2.40%)
reference [21]	9.29	12.19	20.51	12.23	12.82	13.41 (4.10%)

	DMPC					
	N	P	G	C	W	average
DPPC-optimised	3.84	4.61	8.59	4.94	6.81	5.76 (1.85%)
DMPC-optimised	4.28	4.15	7.62	5.49	6.51	5.61 (1.81%)
DOPC-optimised	5.89	8.81	13.44	8.29	7.74	8.83 (2.87%)
DSPC-optimised	5.60	7.90	11.63	6.51	6.29	7.58 (2.45%)
reference [21]	8.53	10.54	13.32	10.00	14.64	11.41 (3.63%)

Transferability

	DPPC					
	N	P	G	C	W	average
DPPC-optimised	4.65	4.10	6.52	7.26	8.91	6.29 (1.71%)
DMPC-optimised	4.45	4.05	6.44	8.37	8.36	6.34 (1.97%)
DOPC-optimised	5.39	8.15	12.05	9.81	6.51	8.38 (2.61%)
DSPC-optimised	5.02	6.08	8.71	9.40	9.63	7.76 (2.40%)
reference [21]	9.29	12.19	20.51	12.23	12.82	13.41 (4.10%)

	DMPC					
	N	P	G	C	W	average
DPPC-optimised	3.84	4.61	8.59	4.94	6.81	5.76 (1.85%)
DMPC-optimised	4.28	4.15	7.62	5.49	6.51	5.61 (1.81%)
DOPC-optimised	5.89	8.81	13.44	8.29	7.74	8.83 (2.87%)
DSPC-optimised	5.60	7.90	11.63	6.51	6.29	7.58 (2.45%)
reference [21]	8.53	10.54	13.32	10.00	14.64	11.41 (3.63%)

Transferability

	DOPC					
	N	P	G	C	W	average
DPPC-optimised	3.28	4.55	6.27	7.59	8.55	6.05 (2.03%)
DMPC-optimised	3.77	3.61	5.44	8.87	7.22	6.78 (1.96%)
DOPC-optimised	3.21	3.37	5.11	8.41	8.63	5.74 (1.95%)
DSPC-optimised	3.21	2.98	5.25	8.80	10.58	6.16 (2.08%)
reference [21]	10.33	6.21	13.38	13.98	24.26	13.63 (4.79%)

	DSPC					
	N	P	G	C	W	average
DPPC-optimised	4.24	3.98	5.13	6.56	11.04	6.19 (1.86%)
DMPC-optimised	4.40	3.52	4.55	7.25	11.59	6.26 (1.88%)
DOPC-optimised	4.90	4.03	5.06	7.36	10.82	6.43 (1.94%)
DSPC-optimised	4.45	3.38	4.17	6.75	11.22	5.99 (1.80%)
reference [21]	8.60	10.30	11.52	10.85	22.62	12.78 (3.80%)

Transferability

	DOPC					
	N	P	G	C	W	average
DPPC-optimised	3.28	4.55	6.27	7.59	8.55	6.05 (2.03%)
DMPC-optimised	3.77	3.61	5.44	8.87	7.22	6.78 (1.96%)
DOPC-optimised	3.21	3.37	5.11	8.41	8.63	5.74 (1.95%)
DSPC-optimised	3.21	2.98	5.25	8.80	10.58	6.16 (2.08%)
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reference [21]	8.60	10.30	11.52	10.85	22.62	12.78 (3.80%)

Summary

- Our machine learning scheme systematically improves on interaction parameters used in the hPF literature
- Makes possible systematic development of accurate and reproducible parameter sets without the need for human fine-tuning
- Less important parameters may be identified on the fly and dropped from the optimization, thus drastically lowering the computational cost (with little impact on the resulting parameter set)
- The optimized potentials show excellent transferability among chemically similar moieties

Acknowledgements

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Hylleraas

UiO

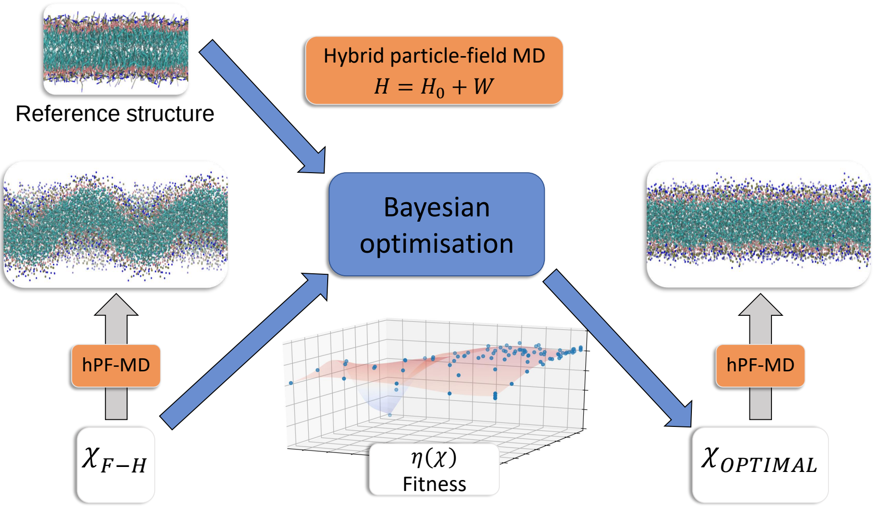
Norwegian Centre of Excellence
The Research Council of Norway

OCCAM
Molecular Dynamics

notur

DFG Deutsche Forschungsgemeinschaft
German Research Foundation

Outline


Reference structure
Hybrid particle-field MD
$H = H_0 + W$
Bayesian optimisation
hPF-MD
χ_{F-H}
$\eta(\chi)$
Fitness
hPF-MD
$\chi_{OPTIMAL}$