

Monte Carlo Methods and Partial Differential Equations: Algorithms and Implications for High-Performance Computing

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Outline of the Talk

Monte Carlo Methods for PDEs

A Little History on Monte Carlo Methods for PDEs

Some Examples Using This for Computing Elliptic Problems

The Walk on Spheres Method

Parallelization

Architectural Implications

Random Number Considerations

Problems in Electrostatics/Materials

Various Acceleration Techniques for Elliptic PDEs

Biochemical Problems

Monte Carlo Estimates

Monte Carlo Estimates

Computational Geometry

Correlated and Uncorrelated Sampling

Computational Results

Conclusions and Future Work

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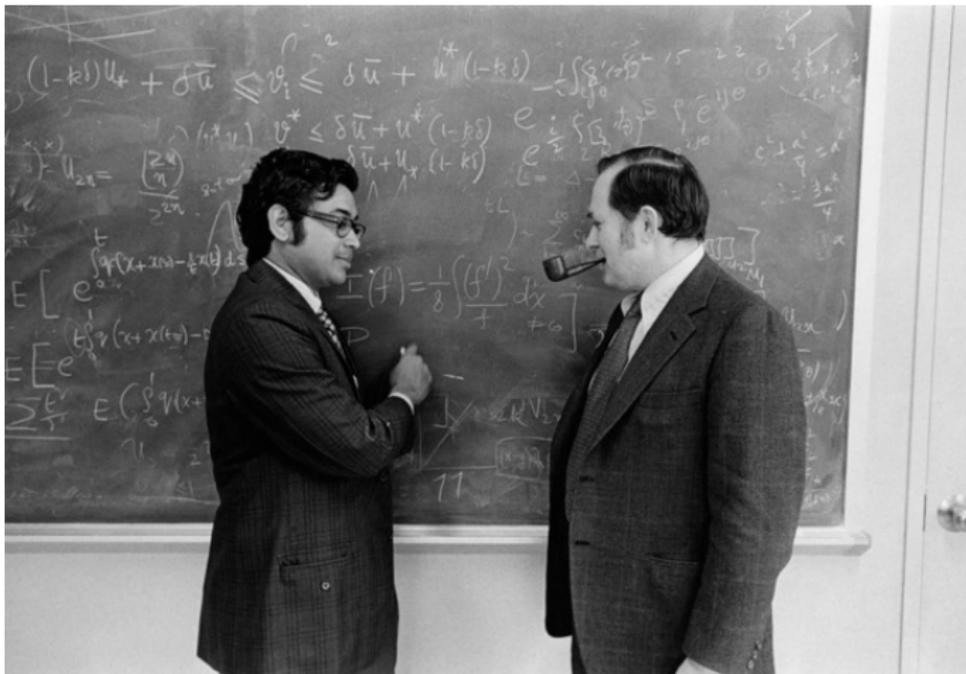
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Dedicated to My Probability Professors at Courant: Raghu Varadhan and Monroe Donsker



Early History of MCMs for PDEs

1. Courant, Friedrichs, and Lewy: Their pivotal 1928 paper has probabilistic interpretations and MC algorithms for linear elliptic and parabolic problems
2. Fermi/Ulam/von Neumann: Atomic bomb calculations were done using Monte Carlo methods for neutron transport, their success inspired much post-War work especially in nuclear reactor design
3. Kac and Donsker: Used large deviation calculations to estimate eigenvalues of a linear Schrödinger equation
4. Forsythe and Leibler: Derived a MCM for solving special linear systems related to discrete elliptic PDE problems

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Integration: The Classic Monte Carlo Application

1. Consider computing $I = \int_0^1 f(x) dx$

2. Conventional quadrature methods:

$$I \approx \sum_{i=1}^N w_i f(x_i)$$

- ▶ Standard quadrature is of this form with deterministic error bounds
- ▶ If we hold work, $f(x_i)$, constant as dimension increases we see the MC advantage vs. the curse of dimensionality

3. Monte Carlo method has two parts to estimate a numerical quantity of interest, I

- ▶ The random process/variable: $x_i \sim U[0, 1]$ i.i.d.
- ▶ The estimator or score: $f(x_i)$
- ▶ One averages and uses a confidence interval for an error bound

$$\bar{I} = \frac{1}{N} \sum_{i=1}^N f(x_i), \quad \text{var}(I) = \frac{1}{N-1} \sum_{i=1}^N (f(x_i) - \bar{I})^2 = \frac{1}{N-1} \left[\sum_{i=1}^N f(x_i)^2 - N\bar{I}^2 \right],$$

$$\text{var}(\bar{I}) = \frac{\text{var}(I)}{N}, \quad I \in \bar{I} \pm k \times \sqrt{\text{var}(\bar{I})}$$

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Other Early Monte Carlo Applications

- ▶ Numerical linear algebra based on sums: $S = \sum_{i=1}^M a_i$
 1. Define $p_i \geq 0$ as the probability of choosing index i , with $\sum_{i=1}^M p_i = 1$, and $p_i > 0$ whenever $a_i \neq 0$
 2. Then a_i/p_i with index i chosen with $\{p_i\}$ is an unbiased estimate of S , as $E[a_i/p_i] = \sum_{i=1}^M \left(\frac{a_i}{p_i}\right) p_i = S$
- ▶ Can be used to solve linear systems of the form $x = Hx + b$
- ▶ Consider the linear system: $x = Hx + b$, if $\|H\| = \mathbb{H} < 1$, then the following iterative method converges:

$$x^{n+1} := Hx^n + b, \quad x^0 = 0,$$

and in particular we have $x^k = \sum_{i=0}^{k-1} H^i b$, and similarly the Neumann series converges:

$$N = \sum_{i=0}^{\infty} H^i = (I - H)^{-1}, \quad \|N\| = \sum_{i=0}^{\infty} \|H^i\| \leq \sum_{i=0}^{\infty} \mathbb{H}^i = \frac{1}{1 - \mathbb{H}}$$

- ▶ Formally, the solution is $x = (I - H)^{-1} b$

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More Modern Monte Carlo Applications

- ▶ **Methods for partial differential and integral equations based on random walks/Markov chains (no need to find a discrete approximation to the PDE/IE)**
 1. Integral equation methods are similar in construction to the linear system methods
 2. PDEs can be solved by using the Feynman-Kac formula
 3. Some Monte Carlo methods can now beat deterministic solvers (electrostatics)
- ▶ Efficient methods that exploit fast probabilistic application of a linear operator
- ▶ Modern sampling methods linear algebra (SVD) based loosely on the Johnson-Lindstrauss projection method
- ▶ Generation of random fields
- ▶ Stochastic DEs and PDEs
- ▶ Financial computing
- ▶ Uncertainty quantification (UQ)

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- ▶ Stochastic DEs and PDEs
- ▶ Financial computing
- ▶ Uncertainty quantification (UQ)

More Modern Monte Carlo Applications

- ▶ Methods for partial differential and integral equations based on random walks/Markov chains (no need to find a discrete approximation to the PDE/IE)
 1. Integral equation methods are similar in construction to the linear system methods
 2. PDEs can be solved by using the Feynman-Kac formula
 3. Some Monte Carlo methods can now beat deterministic solvers (electrostatics)
- ▶ Efficient methods that exploit fast probabilistic application of a linear operator
- ▶ Modern sampling methods linear algebra (SVD) based loosely on the Johnson-Lindstrauss projection method
- ▶ Generation of random fields
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The First Passage (FP) Probability is the Green's Function

Back to our canonical elliptic boundary value problem:

$$\begin{aligned}\frac{1}{2}\Delta u(x) &= 0, \quad x \in \Omega \\ u(x) &= f(x), \quad x \in \partial\Omega\end{aligned}$$

- ▶ Distribution of z is uniform on the sphere
- ▶ Mean of the values of $u(z)$ over the sphere is $u(x)$
- ▶ $u(x)$ has mean-value property and harmonic
- ▶ Also, $u(x)$ satisfies the boundary condition

$$u(x) = \mathbb{E}_x[f(X^x(t_{\partial\Omega}))] \tag{1}$$

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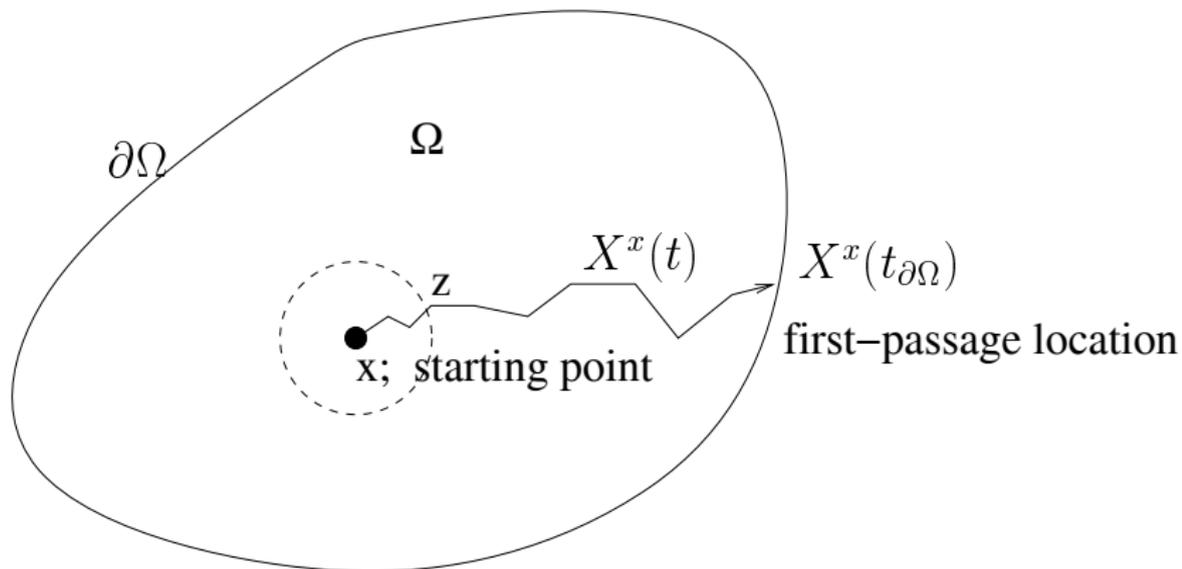
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Reinterpreting as an average of the boundary values

$$u(x) = \int_{\partial\Omega} p(x, y) f(y) dy \quad (2)$$

Another representation in terms of an integral over the boundary

$$u(x) = \int_{\partial\Omega} \frac{\partial g(x, y)}{\partial \mathbf{n}} f(y) dy \quad (3)$$

$g(x, y)$ – Green's function of the Dirichlet problem in Ω

$$\implies p(x, y) = \frac{\partial g(x, y)}{\partial \mathbf{n}} \quad (4)$$

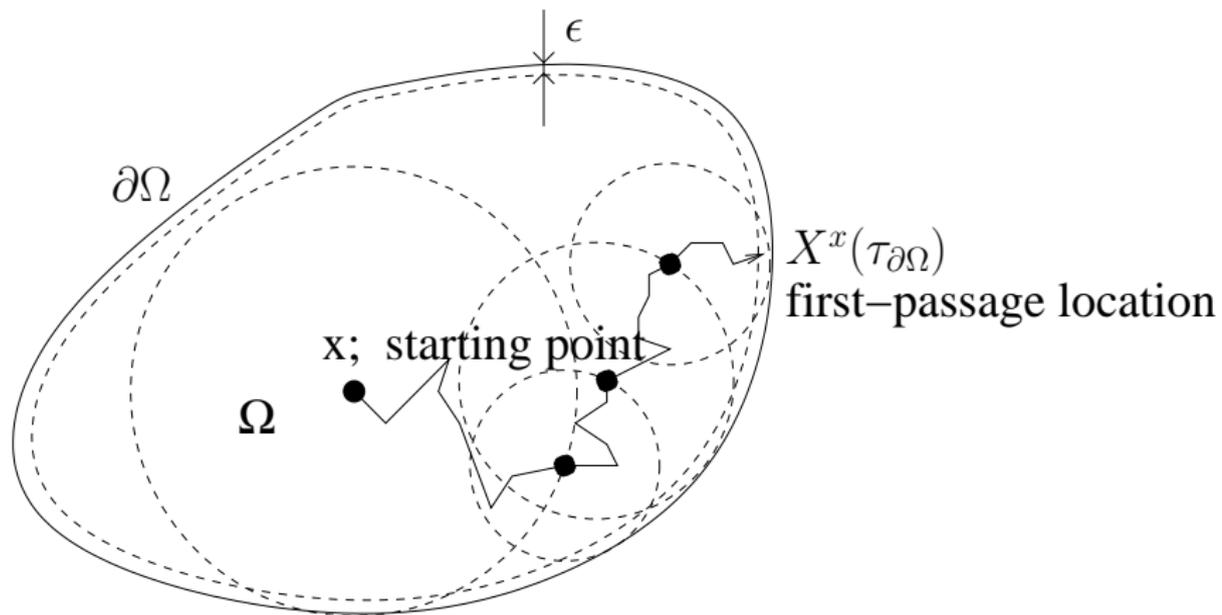
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- ▶ Green's function is known
 - ⇒ direct simulation of exit points and computation of the solution through averaging boundary values
- ▶ Green's function is unknown
 - ⇒ simulation of exit points from standard subdomains of Ω , e.g. spheres
 - ⇒ Markov chain of 'Walk on Spheres' (or GFFP algorithm)
 - $X_0 = X, X_1, \dots, X_N$
 - $x_j \rightarrow \partial\Omega$ and hits ε -shell is $N = O(|\ln(\varepsilon)|)$ steps
 - x_N simulates exit point from Ω with $O(\varepsilon)$ accuracy

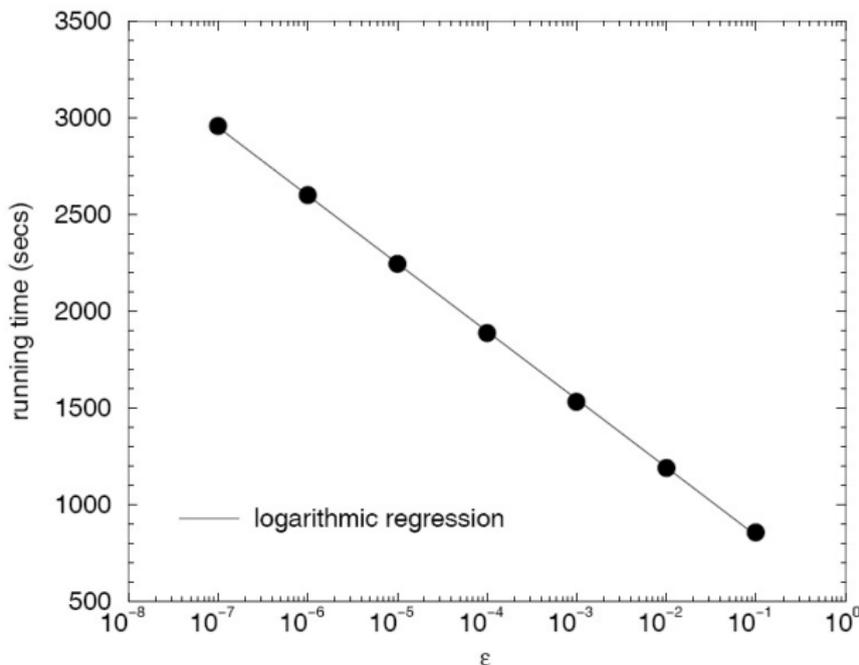
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Timing with WOS



Parallelization of the Monte Carlo Method

- ▶ These Monte Carlo methods are naturally parallel, and have many possible sources of independent parallel work due to their sampling nature
- ▶ Parallelization based on processing different samples that can almost always be executed without decomposition and hence communication
- ▶ In integration can parallelize based on
 1. Sample numbers (with different RNG streams)
 2. Domain decomposition
 3. Can have adaptivity with only the cost of some initial variance estimation
- ▶ Only the final sample (1 integer, 2 reals) needs to be asynchronously communicated to compute the overall mean and variance, very cheap application-level checkpointing

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Memory and Communication

- ▶ Often the Monte Carlo method deals with the geometry without discretization, much less memory is needed to represent the entire problem
- ▶ Mean and variance are computed by calculating a running (1) sum, (2) sum of squares, and (3) samples
- ▶ Independent sampling means that one can do AS MUCH computation per core as you wish before even these three values need be communicated (tuning the level of compute-boundedness)
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Architectural Considerations

- ▶ **Some trends in HPC architectures**
 1. Memory per processor/core has inflected and is now decreasing
 2. Long-term trend is that memory bandwidth is the limiting factor for performance and cost
 3. High clock rates and high bandwidth communication lead to high energy consumption and hot boxes that need cooling
- ▶ These Monte Carlo algorithms avoid all three of issues due to their innate performance
 1. Minimal memory usage has always been a benefit of Monte Carlo methods
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All This Depends on High-Quality Pseudorandom Number Generators

- ▶ The ability of a Monte Carlo method to work depends on the quality random numbers used
- ▶ In a serial application, this is essentially the ability of a pseudorandom number generator to pass an extensive suite of test of randomness (mostly statistical)
- ▶ For good parallel performance, the streams used in each independent realization must lead to qualitatively independent sampling
 1. Must be free if intra- and inter-stream correlations
 2. Must be able to supply potentially very long computations
- ▶ There are very few packages available that even attempt to provide this functionality
 1. Scalable Parallel Random Number Generators (SPRNG) library
 2. TINA Is No Acronym (TINA)
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Porous Media: Complicated Interfaces



Computing Capacitance Probabilistically

- ▶ Hubbard-Douglas: can compute permeability of nonskew object via capacitance
- ▶ Recall that $C = \frac{Q}{U}$, if we hold conductor (Ω) at unit potential $u = 1$, then $C =$ total charge on conductor (surface)
- ▶ The PDE system for the potential is

$$\Delta u = 0, \quad x \notin \Omega; \quad u = 1, \quad x \in \partial\Omega; \quad u \rightarrow 0 \quad \text{as } |x| \rightarrow \infty \quad (5)$$

- ▶ Recall $u(\mathbf{x}) = \mathbb{E}_x[f(X^x(t_{\partial\Omega}))]$ = probability of walker starting at \mathbf{x} hitting Ω before escaping to infinity
- ▶ Charge density is first passage probability
- ▶ Capacitance (relative to a sphere) is probability of walker starting at \mathbf{x} (random chosen on sphere) hitting Ω before escaping to infinity

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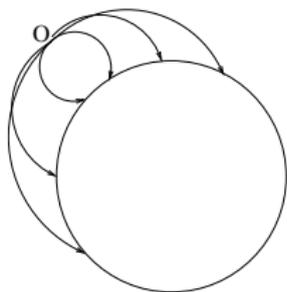
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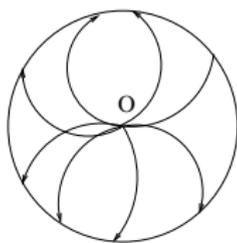
$$\Delta u = 0, \quad x \notin \Omega; \quad u = 1, \quad x \in \partial\Omega; \quad u \rightarrow 0 \quad \text{as } |x| \rightarrow \infty \quad (5)$$

- ▶ Recall $u(\mathbf{x}) = \mathbb{E}_{\mathbf{x}}[f(X^{\mathbf{x}}(t_{\partial\Omega}))]$ = probability of walker starting at \mathbf{x} hitting Ω before escaping to infinity
- ▶ Charge density is first passage probability
- ▶ Capacitance (relative to a sphere) is probability of walker starting at \mathbf{x} (random chosen on sphere) hitting Ω before escaping to infinity

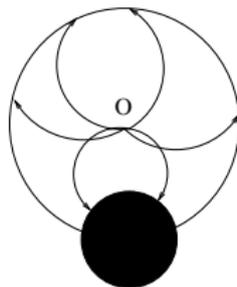
Various Laplacian Green's Functions for Green's Function First Passage (GFFP)



(a) Putting back



(b) Void space



(c) Intersecting

Escape to ∞ in A Single Step

- ▶ Probability that a diffusing particle at $r_0 > b$ will escape to infinity

$$P_{esc} = 1 - \frac{b}{r_0} = 1 - \alpha \quad (6)$$

- ▶ Putting-back distribution density function

$$\omega(\theta, \phi) = \frac{1 - \alpha^2}{4\pi[1 - 2\alpha \cos \theta + \alpha^2]^{3/2}} \quad (7)$$

- ▶ (b, θ, ϕ) ; spherical coordinates of the new position when the old position is put on the polar axis

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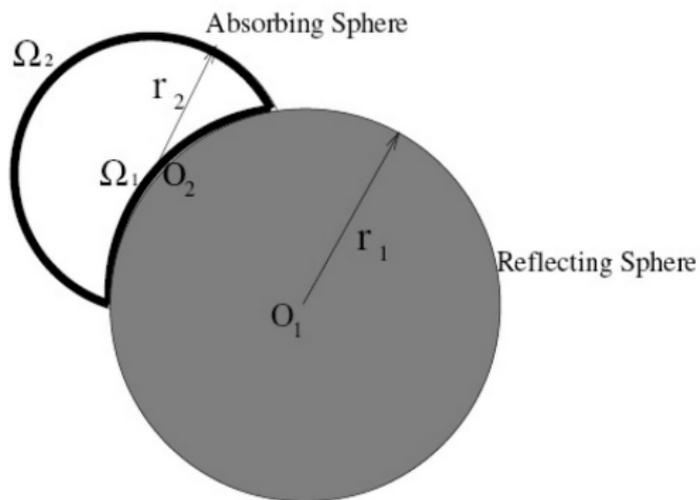
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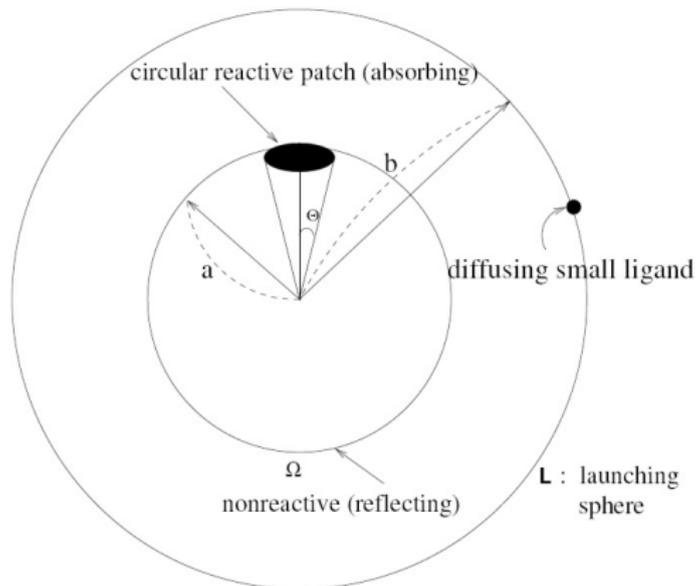
The Simulation-Tabulation (S-T) Method for Generalization

- ▶ Green's function for the non-intersected surface of a sphere located on the surface of a reflecting sphere



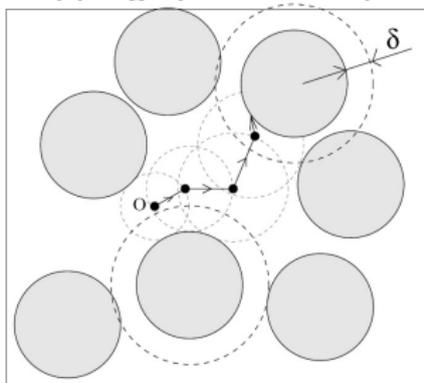
Solc-Stockmayer Model without Potential

Basic model for diffusion-limited protein-ligand binding



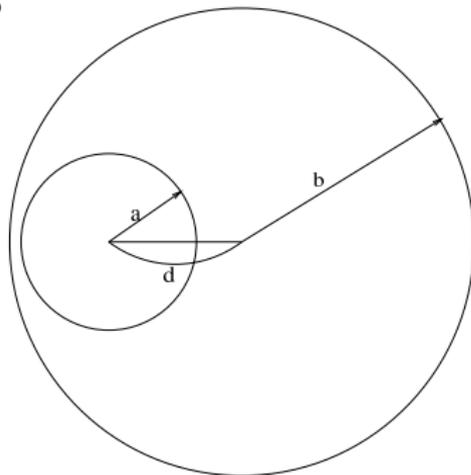
Another S-T Application: Mean Trapping Rate

In a domain of nonoverlapping spherical traps :

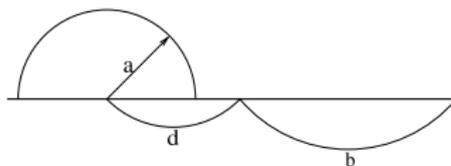


Charge Density on a Circular Disk via Last-Passage

From the top

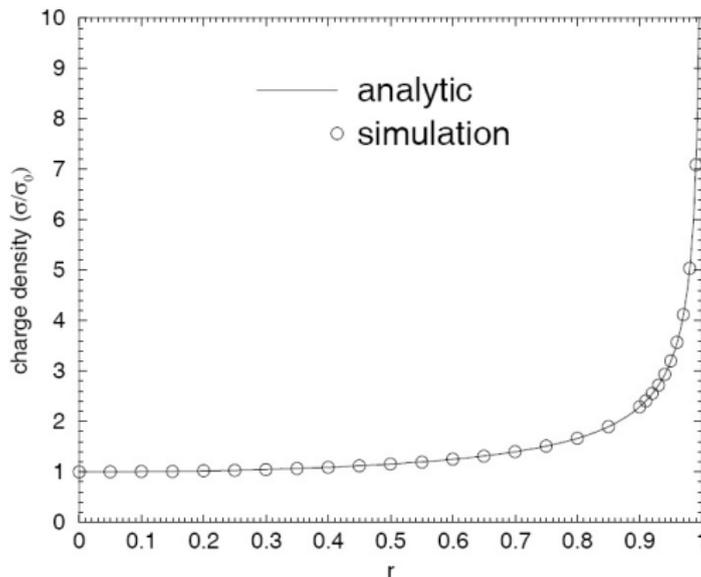


From the side



Charge Density on the Circular Disk

charge density on a circular disk



Unit Cube Edge Distribution

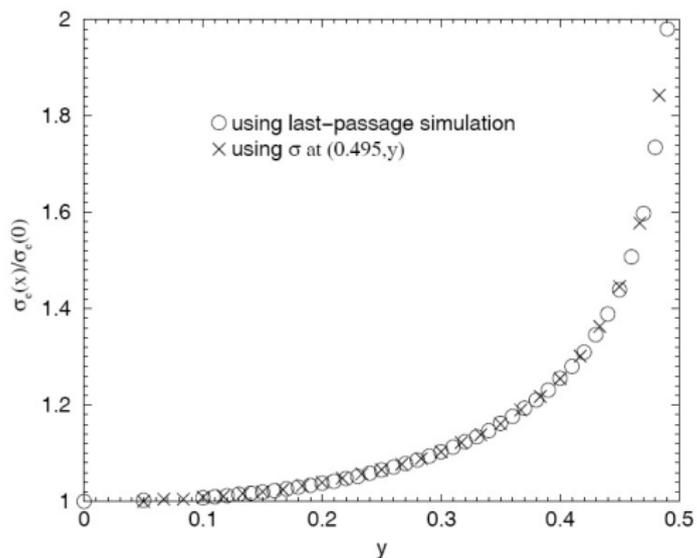


Figure: First- and last-passage edge computations

Walk on the Boundary Algorithm

- ▶ $\mu(y) = -\frac{1}{4\pi} \frac{\partial \phi}{\partial n}(y)$; surface charge density
- ▶ $\phi(x) = \int_{\partial\Omega} \frac{1}{|x-y|} \mu(y) d\sigma(y)$; electrostatic potential

Limit properties of the normal derivative ($x \rightarrow y$ outside of Ω):

$$\mu(y) = \int_{\partial\Omega} \frac{n(y) \cdot (y - y')}{2\pi|y - y'|^3} \mu(y') d\sigma(y')$$

By the ergodic theorem (convex Ω)

$$\int_{\partial\Omega} v(y) \pi_{\infty}(y) d\sigma(y) = \lim_{N \rightarrow \infty} \frac{1}{N} \sum_{n=1}^N v(y_n)$$

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- ▶ π_∞ - stationary distribution of Markov chain $\{y_n\}$ with transition density $p(y_n \rightarrow y_{n+1}) = \frac{n(y_{n+1}) \cdot (y_{n+1} - y_n)}{2\pi|y_{n+1} - y_n|^3}$
- ▶ $\mu = C\pi_\infty$
- ▶ C - capacitance if $\phi|_{\partial\Omega} = 1$
- ▶ $\phi(x) = 1$ for $x \in \Omega$

$$C = \left(\lim_{N \rightarrow \infty} \frac{1}{N} \sum_{n=1}^N v(y_n) \right)^{-1} \quad \text{for} \quad v(y) = \frac{1}{x - y}$$

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Capacitance of the Unit Cube

Reitan-Higgins (1951)	0.6555
Greenspan-Silverman (1965)	0.661
Cochran (1967)	0.6596
Goto-Shi-Yoshida (1992)	$0.6615897 \pm 5 \times 10^{-7}$
Conjectured Hubbard-Douglas (1993)	0.65946...
Douglas-Zhou-Hubbard (1994)	0.6632 ± 0.0003
Given-Hubbard-Douglas (1997)	0.660675 ± 0.00001
Read (1997)	0.6606785 ± 0.000003
First passage method (2001)	0.660683 ± 0.000005
Walk on boundary algorithm (2002)	0.6606780 ± 0.0000004

Continuum Biochemical Electrostatics

Motivation

- ▶ **Experimental Data:** Folding, stability & binding behavior of biomolecules can be modulated by changes in salt concentration
- ▶ **Physical Model:** Implicit solvent-based Poisson-Boltzmann model can provide accurate predictions of salt dependent behavior of biomolecules
- ▶ **Mathematical Model:** Elliptic boundary-value problems

Specific Problems

- ▶ Electrostatic free energy for linear case: only finite number of electrostatic potential point values
- ▶ Dependence of energy on geometry: needs accurate treatment
- ▶ Singularities in solution: have to be taken into account analytically
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Mathematical Model: Molecular Geometry

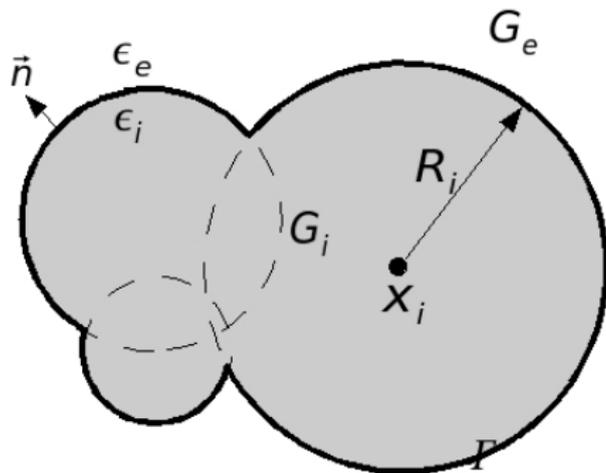


Figure: Biomolecule with dielectric ϵ_i and region region G_i is in solution with dielectric ϵ_e and region G_e . On the boundary of the biomolecule, electrostatic potential and normal component of dielectric displacement continue

Mathematical Model: Partial Differential Equations

- ▶ Poisson equation for the electrostatic potential, Φ_i , and point charges, Q_m , inside a molecule (in CGS units):

$$\epsilon_i \Delta \Phi_i(x) + 4\pi \sum_{m=1}^M Q_m \delta(x - x^{(m)}) = 0, \quad x \in G_i$$

- ▶ For 1-1 salt (such as *NaCl*) Poisson-Boltzmann equation (PBE):

$$\Delta \Phi_e(x) - \kappa^2 \sinh(\Phi_e(x)) = 0, \quad x \in G_e,$$

but we only consider the linearized PBE:

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- ▶ For one-surface model: continuity condition on the dielectric boundary

$$\Phi_i = \Phi_e, \quad \epsilon_i \frac{\partial \Phi_i}{\partial n(y)} = \epsilon_e \frac{\partial \Phi_e}{\partial n(y)}, \quad y \in \Gamma$$

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Electrostatic Potential and Energy

- ▶ Point values of the potential: $\Phi(x) = \Phi_{rf}(x) + \Phi^c(x)$
Here, singular part of Φ :

$$\Phi^c(x) = \sum_{m=1}^M \frac{Q_m}{|x - x^{(m)}|}$$

- ▶ Reaction field electrostatic free energy of a molecule is linear combination of point values of the regular part of the electrostatic potential:

$$W_{rf} = \frac{1}{2} \sum_{m=1}^M \Phi_{rf}(x^{(m)}) Q_m ,$$

- ▶ Electrostatic solvation free energy = difference between the energy for a molecule in solvent with a given salt concentration and the energy for the same molecule in vacuum:

$$\Delta G_{Solv}^{elec} = W_{rf}(\epsilon_i, \epsilon_e, \kappa) - W_{rf}(\epsilon_i, 1, 0)$$

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- ▶ If we set $f(x) = 0$ and have $g(x) \neq 0$, the solution is

$$u(y) = \mathbb{E} \left[\int_0^{\tau_{\partial\Omega}} g(\beta_y(s)) ds \right]$$

- ▶ By linear superposition, the solution to Poisson equation is given probabilistically as

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'Walk-on-Spheres' Algorithm

- ▶ Walk-on-spheres (WOS) algorithm for general domains with a regular boundary
- ▶ Define a Markov chain $\{x_i, i = 1, 2, \dots\}$
- ▶ Set $x_0 = x^{(m)}$ for some m , $x_i = x_{i-1} + d_i \omega_i$, $i = 1, 2, \dots$, where
 1. $d_i = d(x_{i-1})$ is distance from x_{i-1} to Γ
 2. $\{\omega_i\}$ is sequence of independent unit isotropic vectors
 3. x_i is the exit point from the ball, $B(x_{i-1}, d(x_{i-1}))$, for a Brownian motion starting at x_{i-1}
- ▶ Outside the molecule, on every step, walk-on-spheres terminates with probability $1 - q(\kappa, d_i)$, where $q(\kappa, d_i) = \frac{\kappa d_i}{\sinh(\kappa d_i)}$ to deal with LPBE

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- ▶ Outside the molecule, on every step, walk-on-spheres terminates with probability $1 - q(\kappa, d_i)$, where $q(\kappa, d_i) = \frac{\kappa d_i}{\sinh(\kappa d_i)}$ to deal with LPBE

'Walk-on-Spheres' Algorithm

- ▶ Walk-on-spheres (WOS) algorithm for general domains with a regular boundary
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'Walk-on-Spheres' and 'Walk-in-Subdomains'

- ▶ For general domains, an efficient way to simulate exit points is a combination of
 1. Inside the molecule: 'walk-in-subdomains'
 2. Outside the molecule 'walk-on-spheres'
- ▶ The whole domain, G_i , is represented as a union of intersecting subdomains:

$$G_i = \bigcup_{m=1}^M G^m$$

- ▶ 'Walk-in-Subdomains': Simulate exit point separately in every G^m
 1. $x_0 = x, x_1, \dots, x_N$ – Markov chain, every x_{i+1} is an exit point from the corresponding subdomain for Brownian motion starting at x_i
 2. For spherical subdomains, $B(x_i^m, R_i^m)$, exit points are distributed in accordance with the Poisson kernel:

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Monte Carlo Estimates

- ▶ The estimate for the reaction-field potential point value:

$$\begin{aligned} \xi[\Phi_{rf}](x^{(m)}) &= -\Phi^c(x_1^*) \\ &+ \sum_{j=2}^{N_{ins}} F_j(\kappa) (\Phi^c(x_j^{ins}) - \Phi^c(x_{j,ins}^*)) \end{aligned} \quad (8)$$

- ▶ Here $\{x_{j,ins}^*\}$ is a sequence of boundary points, after which the random walker moves inside the domain, G_i , to x_j^{ins}
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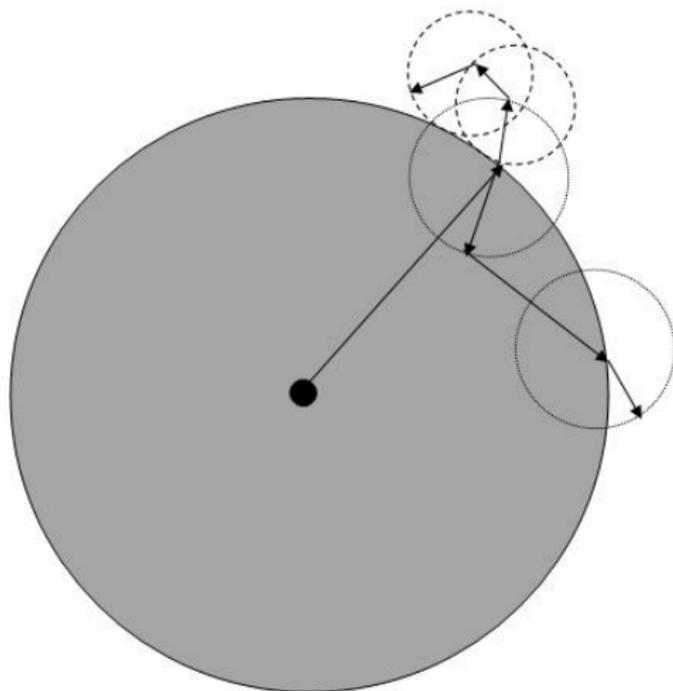
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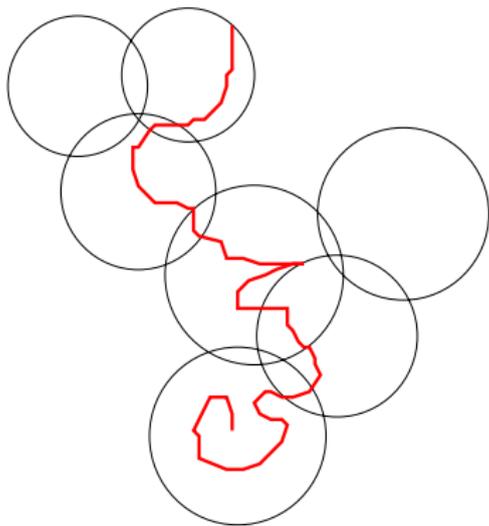
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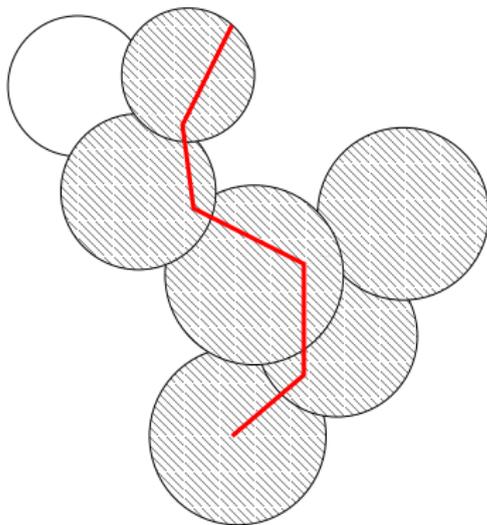
A Picture: The Algorithm for a Single Spherical Atom



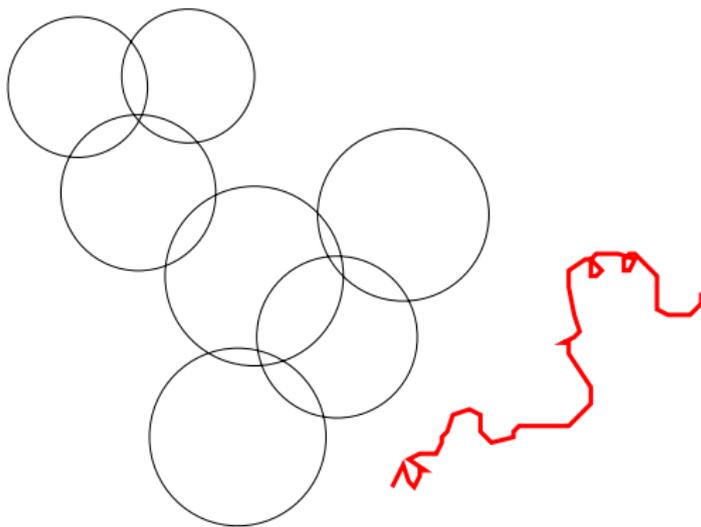
The Algorithm in Pictures: Walk Inside



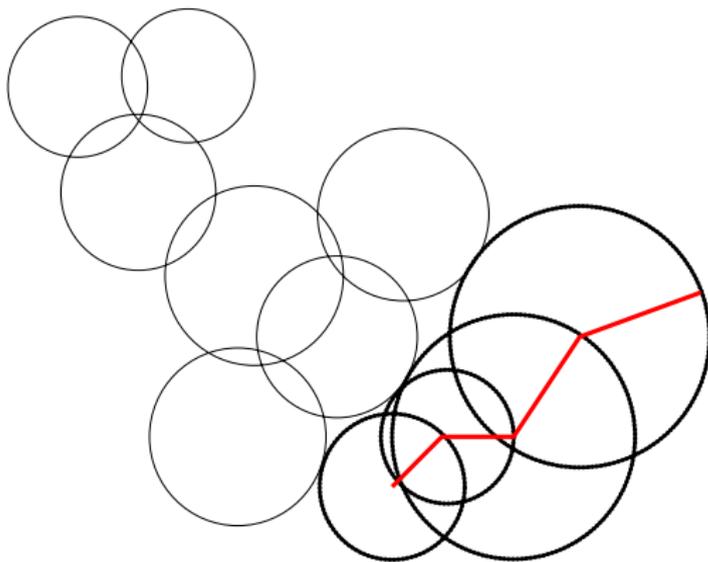
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The Algorithm in Pictures: Walk Outside



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Monte Carlo Algorithm's Computational Complexity

Cost of a single trajectory

- ▶ Number of steps in random walk is not dependent on M , the number of atoms
- ▶ The cost of finding the nearest sphere is $M \log_2(M)$ due to optimizations

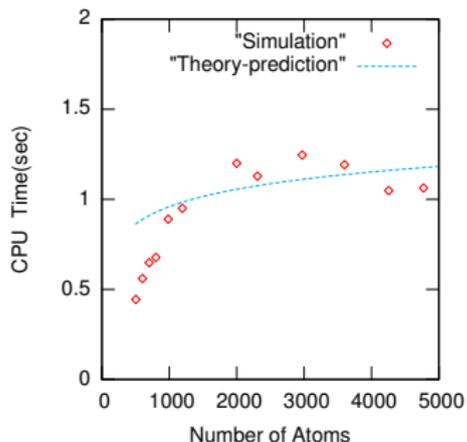


Figure: The CPU time per atom per trajectory is plotted as function of number of atoms. For small number of atoms the CPU time scales linearly and for large number of atoms it asymptotically scales logarithmically

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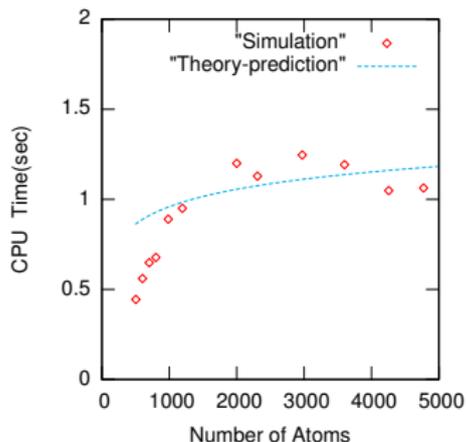


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Geometry: Problem Descriptions

There are many geometric problems that arise in this algorithm:

- ▶ Efficiently determining if a point is on the surface of the molecule or inside of it (for interior walks)
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Correlated and Uncorrelated Sampling

- ▶ Correlated sampling in Monte Carlo is essential for two important reasons
 1. To obtain smooth curves with a minimum of sampling (function-wise vs. point-wise sampling)
 2. To obtain accurate results from quantities defined as the differences of Monte Carlo estimates
- ▶ With this correlated sampling sampling you can get a “smooth curve” with three orders of magnitude less sampling, note: you still have $O(N^{-1/2})$ errors, just in “curve space,” not point by point

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Correlated Sampling: Salt Concentration

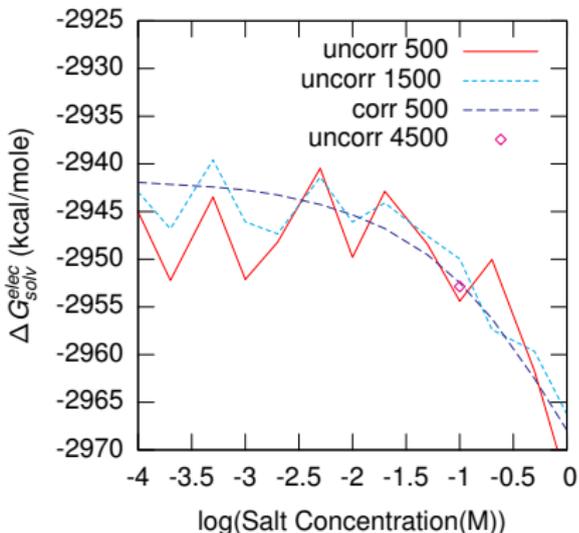


Figure: Electrostatic Solvation free Energy of $3icb$ calculated with three four conditions: uncorrelated sampling with 500 number of trajectories per concentration, uncorrelated sampling with 1500 number of trajectories per concentration, uncorrelated sampling with 4500 number of iterations, and correlated sampling with 500 number of trajectories

Dependence on Salt Concentration

- ▶ Values of scalar energies as a function of external salt concentration are important
 1. Smooth curves of internal energy vs. salt concentration (see above)
 2. Numerical estimate of the derivative as salt concentration vanishes
- ▶ For κ used in simulations, $F_j(\kappa) = 1$
- ▶ For an arbitrary $\kappa' > \kappa$:

$F_j(\kappa')$ is multiplied by the ratio $\frac{q(\kappa', d)}{q(\kappa, d)}$ on every step of the WOS in the exterior
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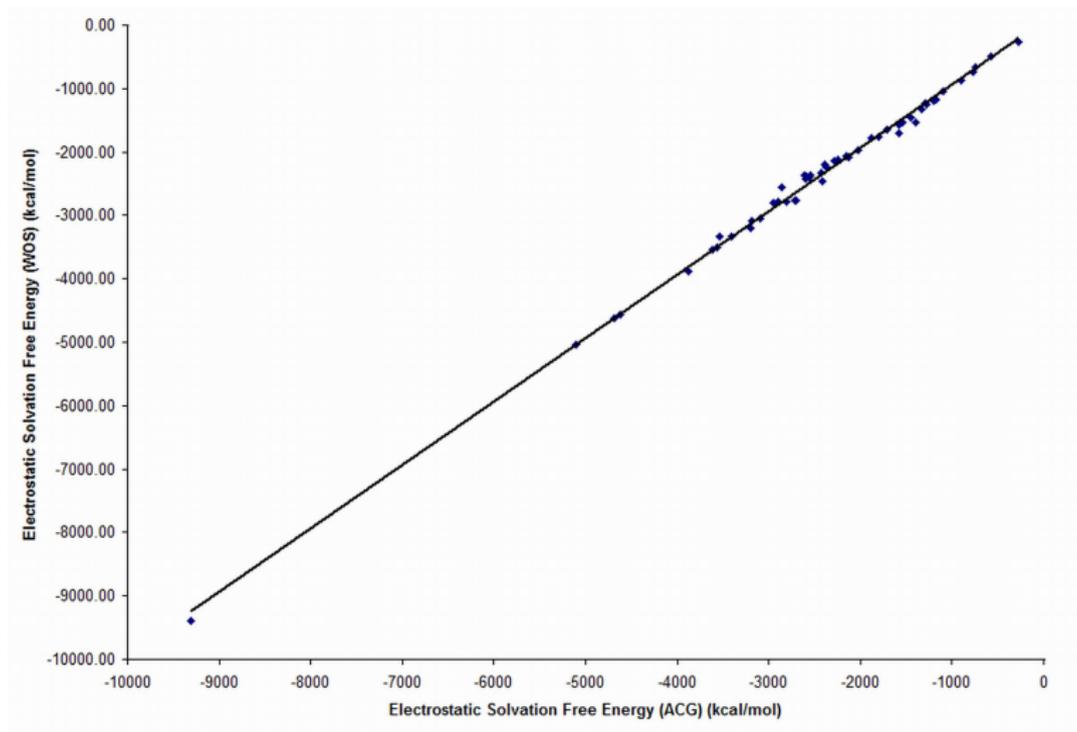
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Accuracy: Monte Carlo vs. Deterministic



Sampling Error and Bias

- ▶ In Monte Carlo there are biases (errors) and sampling error
 1. Sampling error is based on standard error $O(N^{-1/2})$
 2. Difference between expected value and PDE solution is bias
 - ▶ Capture thickness (ϵ): bias is $O(\epsilon)$
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 3. $Var[\sum_i q_i \Phi(x_i)] = \sum_i q_i^2 Var[\Phi(x_i)]$
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 5. Running time $\propto \frac{|\ln(\epsilon)|}{a}$
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 7. Large ANN means errors in drawing the largest sphere outside the molecule for WOS

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 - ▶ Overall bias: $(\frac{a}{2R})^3 + (\frac{\epsilon}{2R})$
 3. $Var[\sum_i q_i \Phi(x_i)] = \sum_i q_i^2 Var[\Phi(x_i)]$
 4. Given a desired variance, divide it evenly over this sum
 5. Running time $\propto \frac{|\ln(\epsilon)|}{a}$
 6. Can reduce running time by 2 orders of magnitude by bias/variance balancing and using larger ϵ , a and ANN
 7. Large ANN means errors in drawing the largest sphere outside the molecule for WOS

Sampling Error and Bias

- ▶ In Monte Carlo there are biases (errors) and sampling error
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Timing: Better Than Expected

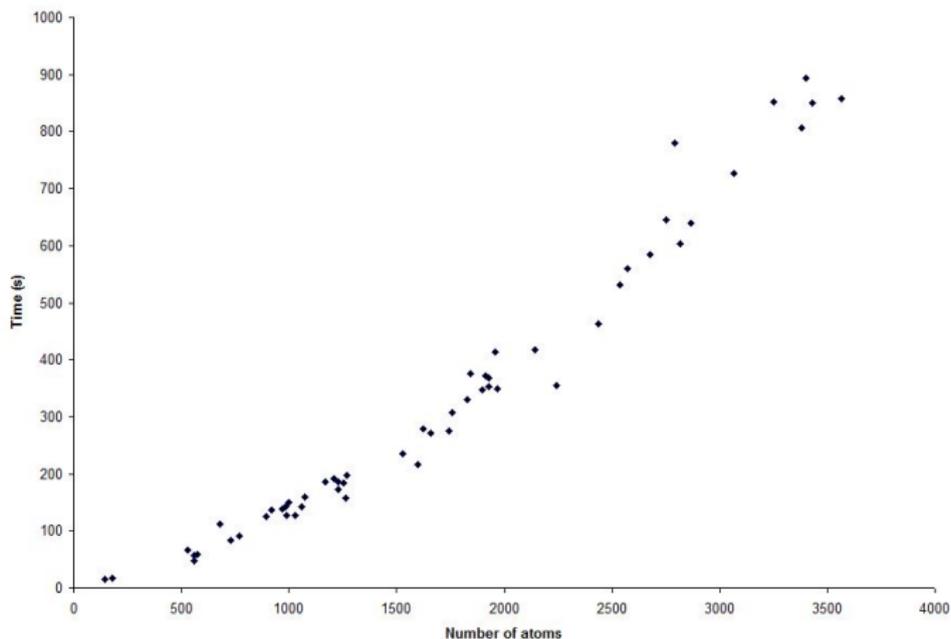


Figure: $O(M \log M)$?

Conclusions

- ▶ Over the years we have developed many MC tools for PDEs and more recently:
- ▶ We have developed a novel stochastic linear PBE solver that can provide highly accurate salt-dependent electrostatic properties of biomolecules in a single PBE calculation
- ▶ Advantages of the stochastic linear PBE solver over the more mature deterministic methods include: the subtle geometric features of the biomolecule can be treated with higher precision, the continuity and outer boundary conditions are accounted for exactly, a singularity free scheme is employed and straightforward implementation on parallel computer platform is possible
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Future Work

- ▶ **Binding computations: using correlated sampling by directly reprocessing walks**
- ▶ Simple code interface for distribution with
 1. Desired accuracy as input that allows a precalculation of the number of needed trajectories
 2. Importance sampling for optimal estimation of scalar energy values
 3. Built-in CONDOR support for distribution of concurrent tasks
 4. Multicore distributed computing support for the code: OpenMP/OpenMPI
 5. Precompiled code module distribution to protect IP
 6. Webpage to describe the method and the mathematical background and application
- ▶ Exploit the implicit inverse computation this methods provides
 1. Can do computation without knowing charges until the end (an inverse)
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