Simulations of DNA Condensation

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SIMULATIONS OF DNA CONденSATION

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MICROSCOPY RESULTS: COUNTERIONS

- Multivalent counterions induce collapse of DNA
- Marked coil-globule coexistence for single chains
- Compact structures are toroids or cigars

(YOSHIKAWA AND CO-WORKERS)
DNA IS CONDENSED BY CHANGING SOLVENT FROM WATER TO ALCOHOL

ALL OR NOTHING PROCESS

COMPACT DNA ARE TOROIDS OR CIGAR-SHAPED

(MEL’NIKOV, KHAN ET AL)
DNA COMPACTED BY MULTIVALENT IONS IS DECOMPACTED BY SALT

MICROSCOPY RESULTS: SALT

DNA COMPACTED BY MULTIVALENT IONS IS DECOMPACTED BY SALT

ALL OR NOTHING PROCESS

COMPACT DNA ARE TOROIDS OR CIGAR-SHAPED

(KHAN ET AL)
**EARLIER SIMULATIONS**

**Hamiltonian**

\[ U_0 = U_{\text{bond}} + U_{\text{es}} + U_{\text{hc}} \]

- **Fixed bond length**
- **Explicit electrostatics**

\[ U_{\text{es}} = \sum_{i<j}^{N+N_c} \frac{q_i q_j e^2}{4 \pi \varepsilon_0 |r_i - r_j|} \]

- **Hard spheres**

**Solve with Metropolis Monte Carlo**
SIMULATION RESULTS: COUNTERIONS

Polyelectrolyte conformation:
- Stretched under "normal" conditions
- Large electrostatic interactions lead to collapse - here multivalent ions
- Collapsed PEs are smaller than neutral chains ---> effective attraction
Due to competition effects, salt unfolds chains compacted by multivalent counterions.
SIMULATION RESULTS: SOLVENT

Stretched under “normal” conditions
Large electrostatic interactions lead to collapse - here dielectric constant
Big difference in behaviour of DNA and flexible polyelectrolyte

POLYELECTROLYTE/DNA CONFORMATION

What about stiffness???
CONVERGENCE PROBLEMS

EVOLUTION OF MC SIMULATION OF DNA CONDENSATION (STIFF CHAIN), N=292 WITH TRIVALENT COUNTERIONS (COEXISTENCE)

EXTREMELY LONG WAIT FOR EQUILIBRIUM RESULTS WEEKS/MONTHS
USE FLAT HISTOGRAM MC

Why?
- Gives the free energy directly
- Efficient close to phase transition
- Allows exploration of high energy configurations
- Very effective parallelization (coarse grained)

Main ideas:
- Instead of importance sampling create a flat distribution of the quantity of interest, $p(R_{ee}) = \text{const.}$ (Similar to Wang-Landau)
- Each processor does not have a constant $p$ but the sum over $N_{cpu}$ does
- Correctly done this gives the potential of mean force (POMF) as a function of the quantity of interest, $w(R_{ee})$
USING PARALLEL WANG-LANDAU GIVES MORE THAN 300 TIMES SPEED-UP ON ISIS
FLAT HISTOGRAMS

$N_{\text{CPU}} = 4$

$N_{\text{CPU}} = 32$

SUM IS FLAT BUT NOT ON EVERY NODE
DISTRIBUTED WL: NETWORK ARCHITECTURES

- Mixed environment
- Low-latency
- Fault tolerant
- Equilibrium results

**Distributed Wang-Landau Algorithm, organizational design**

Centralized "server"
- Receives new incoming data, returns summed PMF value $U^*$

- PC/Linux node
- Cluster node
- Mac node

Nodes receive current summed PMF $U^*$ and add new data to the total (e.g., reporting to server every 100 Monte Carlo iterations)

- GPU
- PS3

LUKE CZAPLA & JOHN GRIME
DNA AS A POLYELECTROLYTE WITH INTRINSIC STIFFNESS

TETRAVALENT COUNTERIONS + MONOVALENT SALT

![Graph showing DNA behavior with different salt concentrations](image)

- $R_{ce} / \text{Å}$ vs. $f$
- Three curves with different $l_p^0$ values:
  - $l_p^0 = 120$
  - $l_p^0 = 39$
  - $l_p^0 = 12$

Graph indicates the relationship between DNA compaction and salt concentration.
FLEXIBLE CHAIN

- $f = 0$
- $f = 0.25$
- $f = 0.5$
- $f = 0.75$
- $f = 1$
SEMI-FLEXIBLE CHAIN

![Graph showing the distribution of $R_{cc}$ for different $f$ values.]

- $f=0$
- $f=0.25$
- $f=0.5$
- $f=0.75$
- $f=1$
STIFF CHAIN

![Graph showing the distribution of R_{ee} in Å with different f values: f=0, f=0.25, f=0.5, f=0.75, f=1. The graph includes a peak at R_{ee} around 500 Å for f=1, with other peaks at lower f values.](image)
Like-charged segments of a polyelectrolyte/DNA can have an effective attraction due to ion correlations --- > DNA condensation

Simulations show that chain stiffness lead to coil-globule coexistence
FORCE-EXTENSION CURVES

- Flexible chains
- Semi-stiff chains
- Stiff chains

- WLC for flexible chains
- Force plateaus for stiffer chains
GRAND-CANONICAL SIMULATIONS

Let the amount of 4+ and 1+ fluctuate
Fix chemical potential
GRAND-CANONICAL SIMULATIONS

semi-flexible chains

\[ g(R_g) \]

\[ N_{4+} = 25 \]

\[ \Delta \mu = 7 \, kT \]

\[ R_g (\text{Å}) \]
The coexistence between compact and extended chains is enhanced in the grand canonical ensemble.
SUMMARY

- Like-charged segments of a polyelectrolyte/DNA can have an effective attraction due to ion correlations --> DNA condensation
- Salt reverses DNA condensation due to competition effects
- Free energy calculations makes it possible to simulate first-order-like phase transition of stiff polyelectrolytes/DNA
- Simulation time for each point is 1 week on 24 processors on 2.8GHz Xeon (5.6 CPU months = 16H on 384 CPUs) --> parallelisation is important
- Simulations show that chain stiffness lead to coil-globule coexistence
- The coil-globule coexistence is enhanced by number fluctuations of counterions
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