Modelling of the structural and mechanical properties of living cell cytoskeleton, DNA and proteins

Somiealo Azote

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ASP Alumni 2016

Biography

- 2007-2011: Bachelor degree in physics, University of Lome, Togo
- 2013-2014: Master degree in Mathematical Science from AIMS-Senegal
- 2014-2015: joint Master program between IMSP-Benin and LIPHy of University of Joseph Fourier, Grenoble France
- 2015-2018: PhD in Physics (Biophysics), Stellenbosch University, South Africa

Biography

- 04/2019-06/2019: Part-time lecturer at INSTI-Lokossa of University of Abomey Calavie, Benin
- 07/2019-10/2019: Summer postdoctoral research visit at Brookhaven National Lab (NY-USA)
- 02/2020-10/2020: Lecturer assistant at Université de Lomé, Togo
- 12/2020-Now: On going postdoctoral studies, Ca Foscari University of Venice

My connection with ASP

- Alumni ASP2016 in Kigali, Rwanda
- Heard about ASP through AIMS mailing list
- Learn about particle Physics , computing and applications in medical field

My connection with ASP

- ASP enabled Networking and collaborations
- ASP and Co initiated some covid research projects to which some Alumni (including myself) and students was part (2 articles submitted for publication)
- Wrote grant applications guided by ASP
- Benefit from ASP Mentorship programs
- Selected by ASP for Research visit at BNL

❖ Research visit to BNL

- Worked on a machine learning project
- Got to learn python for the data analysis and classification.
- Very useful contacts
- Pictures of African students visiting BNL under the ASP research program, and the program organisers (staff at BNL)

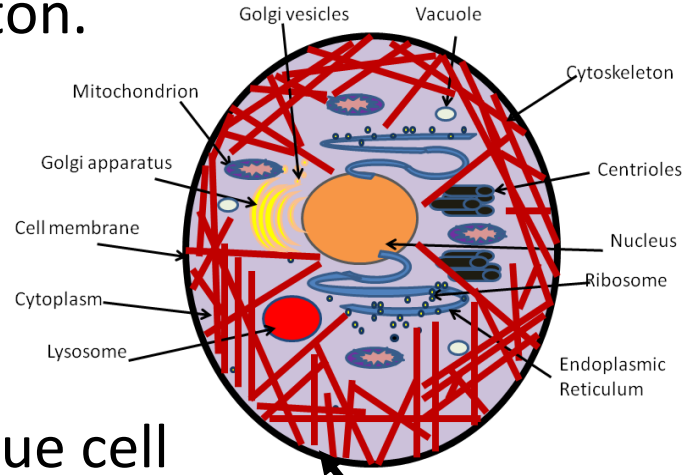
About my previous (PhD) and current research (postdoc)

Overview

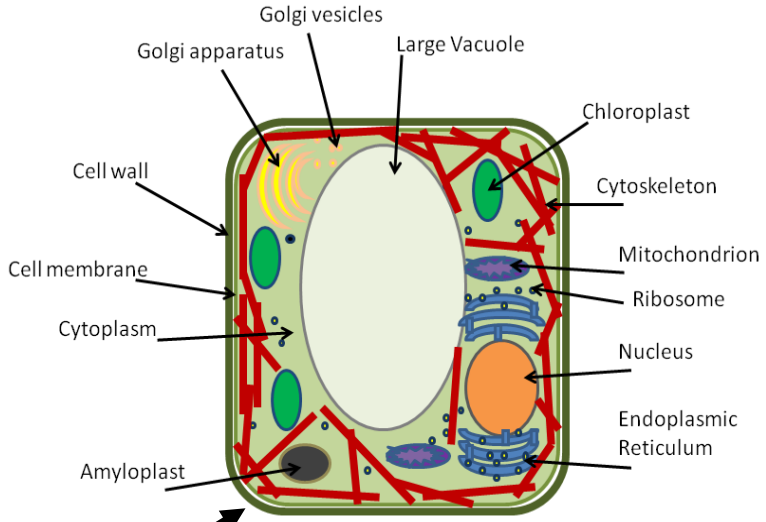
- ➢Part 1: About my PhD work
- ✓ Role of the cytoskeleton in the mechanics of eukaryotic cells
- ✓Introduction to polymers physics
- ✓ Models for confined branching actin networks and results.
- ➢Part 2: Presentation of my current project
- ✓Coarse-grained modelling of DNA and proteins
- ➢Conclusions

Eukaryotic cells

- Plants and animal cells or eukaryotic cells, possess a complex network of filaments called cytoskeleton.



Animal tissue cell



Plant tissue cell

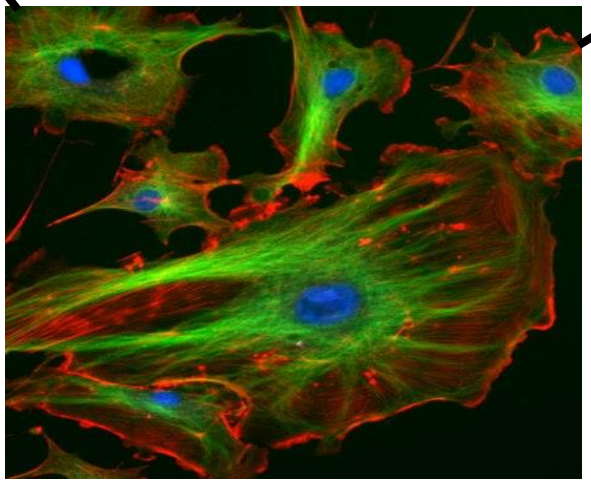
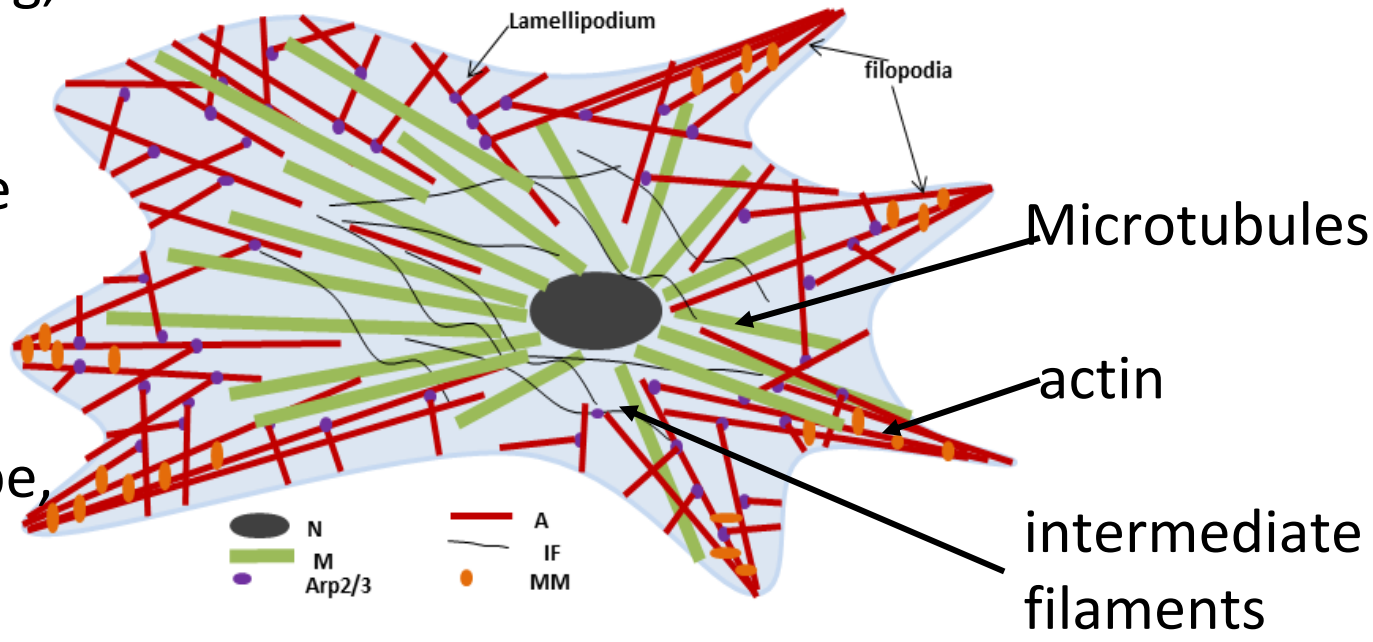


Image of eukaryotic cell cytoskeleton (Wikipedia)

Role of the cytoskeleton in the mechanics of cells

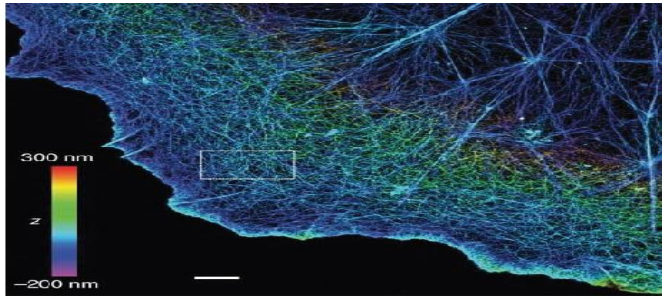
- The cytoskeleton responsible of the cell mechanics (locomotion, wound healing, tissue growth, transport)
- It provide structural support: Hold the organelles in place
- Actin are the most abundant, strengthen and maintain the cell shape, cell division
- Microtubules and actin are semiflexible While intermediate filaments are flexible



Cartoon of the cytoskeleton

Branching actin networks assembly

- Actin networks are the most abundant and highly branched at the edge of the cell.



Ke Xu et al, 2017

Image of branching actin cytoskeleton at the leading edge of the cell

Branching of actin via Arp2/3 protein complex at 70 degree.

- The stability of cells in tissues depend mainly on the elasticity of branching actin networks.

- The elasticity of branching actin networks depends on their topology, orientation and spatial organization

Role of Actin networks

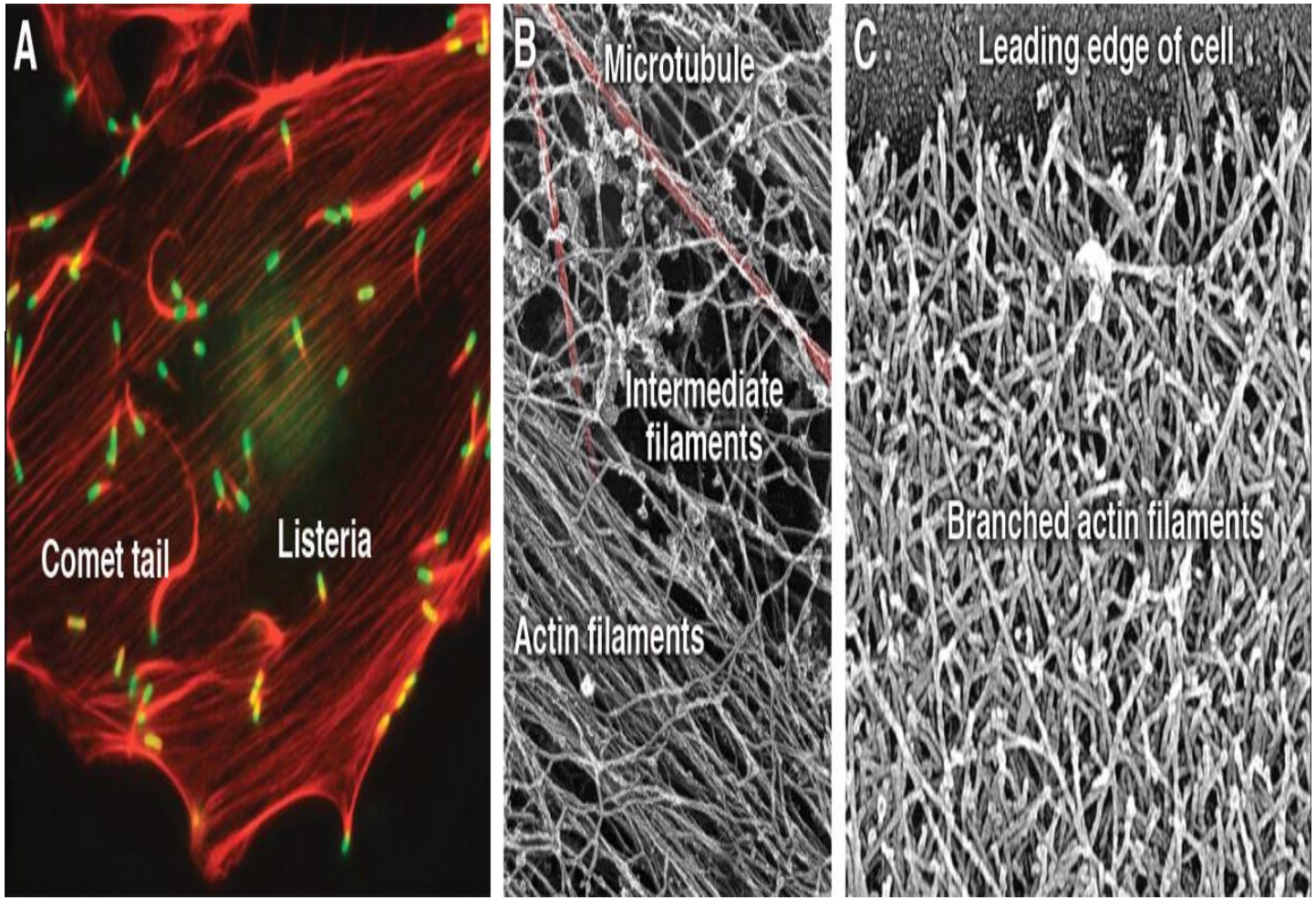
Spatial Cell Biology

REVIEW

Actin, a Central Player in Cell Shape and Movement

Thomas D. Pollard[1]* and John A. Cooper[2]

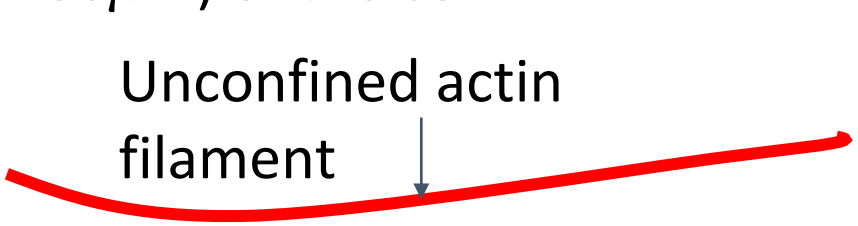
- Some bacteria that lives in animals such Listeria take advantage of the spatial organization and rearrangement of branched actin network at the edge of the cell

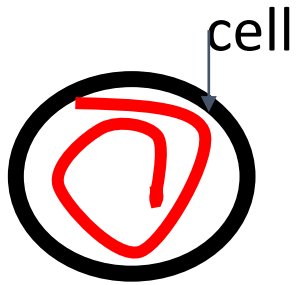


cell membrane confinement effects

- The growth, structure, spatial organisation and orientational ordering of branching actin networks are controlled by the effect of confinement that the cell membrane introduces.

- An actin filament is semiflexible with persistence length (17.7μm) similar to the size (10-100μm) of the cell.

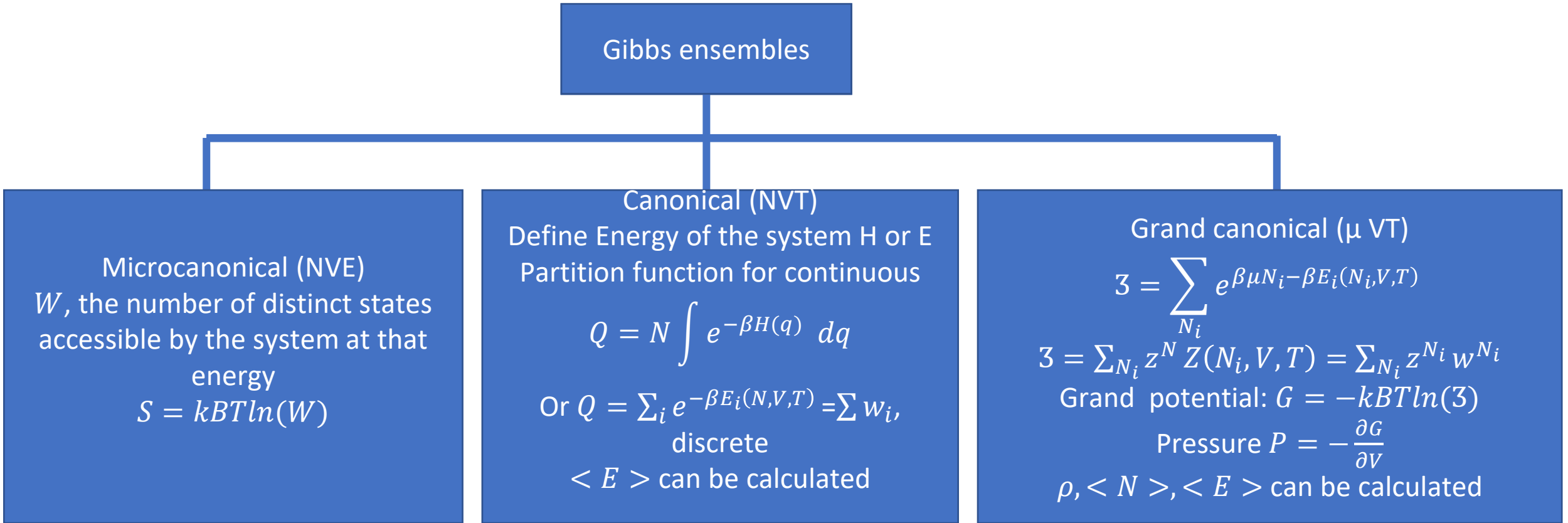




- Semiflexible polymer models with tools from statistical physics can be used to determine the role of geometrical confining parameters in the structural and conformational properties of linear and branching actin filaments.

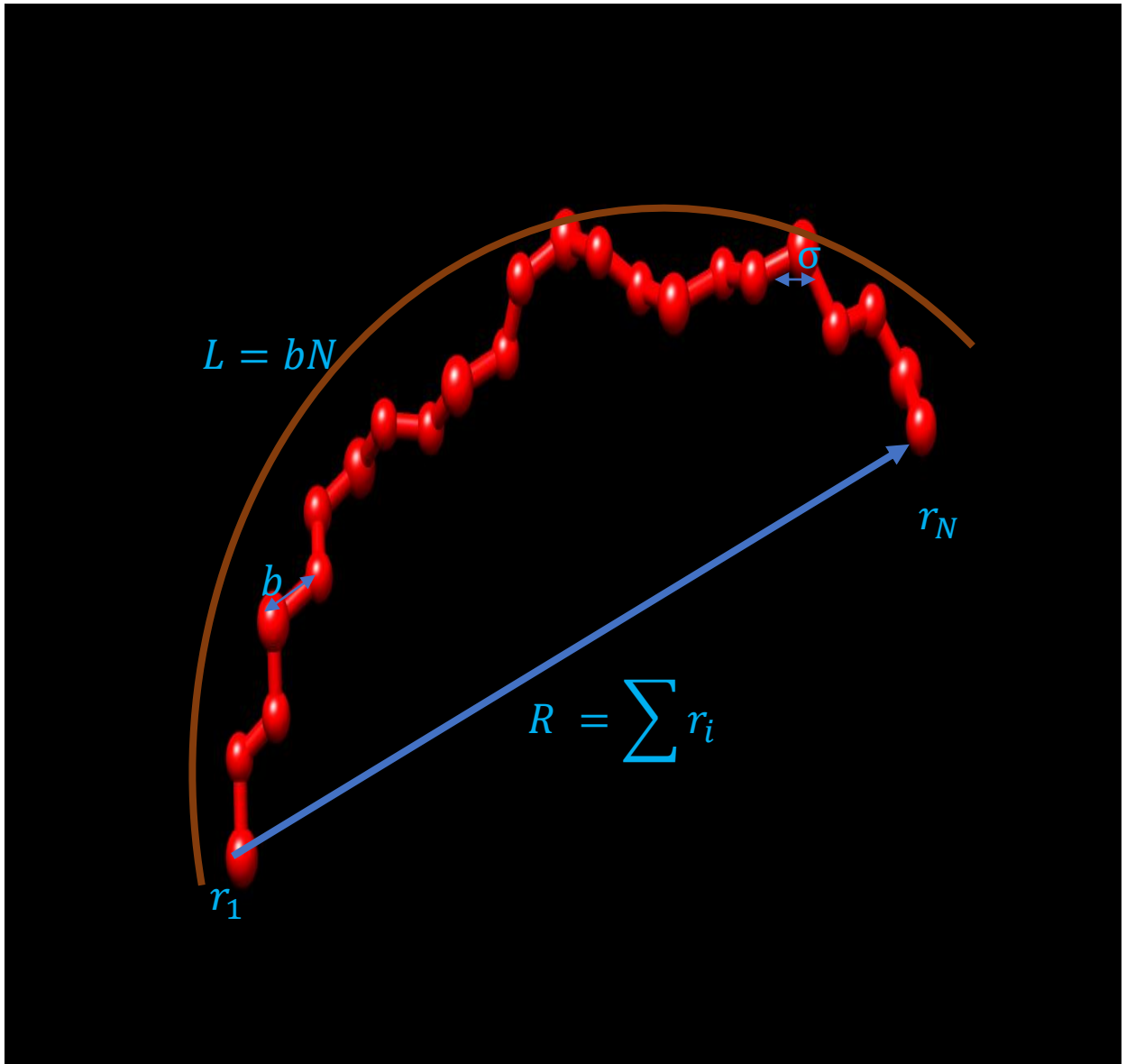
Physics of polymers: statistical mechanics

- Statistical mechanics allows to compute the thermodynamics properties of polymers.
- They describe the structure and dynamics of the polymer
- Depending on the properties one would like to measure, one of the Gibbs ensemble is used.



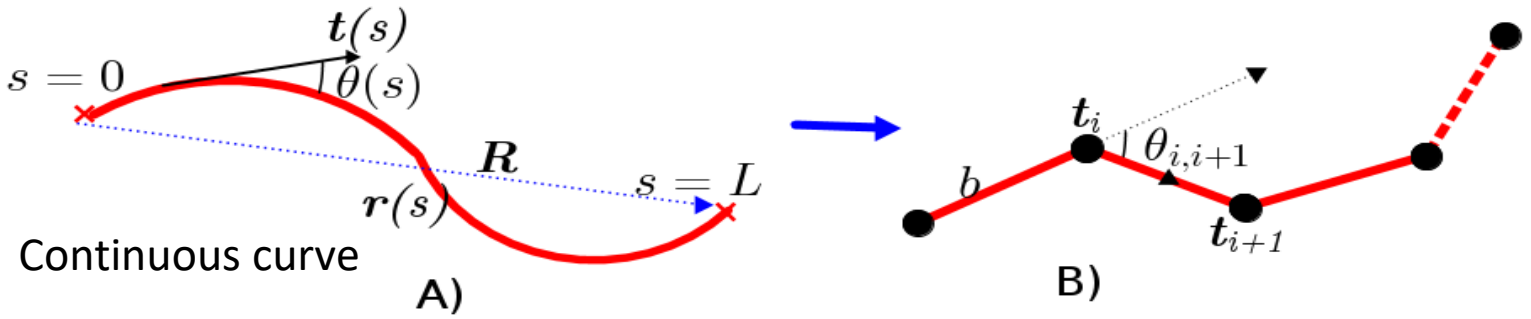
Physics of polymers: Length scales

- Polymer are classified
- Flexible (intermediate filaments) if $L > l_p$
- Semiflexible (microtubule and Actin) if $L \sim l_p$
- Rigid if $L < l_p$



Polymer model for semiflexible (actin) filaments

- Example of coarse-grained polymer model for actin filament (Kratky Porod Worm-like chain models)



The persistence length is given by:

- Canonical partition function

$$< \boldsymbol{t}_i \cdot \boldsymbol{t}_{i+1} >=< \cos(\theta) >= e^{-L/l_p}$$

$$Z = \mathcal{N} \int \mathcal{D}\boldsymbol{r} e^{-\beta H[\boldsymbol{r}]} \delta(\boldsymbol{t^2} - \mathbf{1}) \quad \text{where} \quad H[\boldsymbol{r}(s)] = \frac{k_b}{2} \int_0^L \mathrm{d}s \left(\frac{\mathrm{d}\boldsymbol{t}(s)}{\mathrm{d}s} \right)^2 \text{ with } \quad \boldsymbol{t}(s) = \frac{d\boldsymbol{r}(\boldsymbol{s})}{ds} \qquad (1)$$

- The partition function is used to compute some of the physical quantities of the polymer chain system.
- The constraint of inextensibility make the theory difficult to add confinement.

Modelling confined branching actin networks and results

- Model for Semiflexible linear filament in the grand canonical representation.

PHYSICAL REVIEW E 67, 011801 (2003)

Stiff polymer in monomer ensemble

K. K. Müller-Nedebock,[1,*] H. L. Frisch,[1,2] and J. K. Percus[3,4]
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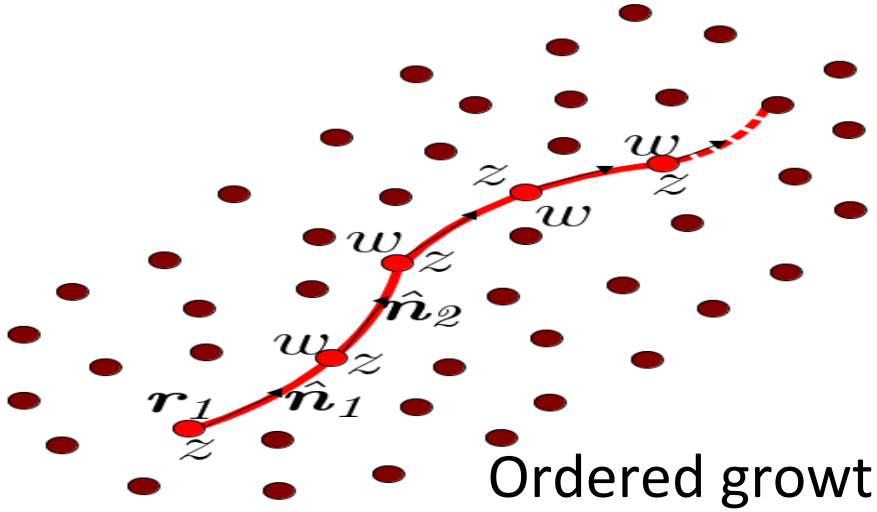
(Received 18 January 2002; revised manuscript received 14 October 2002; published 9 January 2003)

- Extension of the model to confined branching networks.

- Phase diagram describing the structural and conformational properties of confined networks.

Model for linear semiflexible polymer

- Model based on monomer ensemble formalism for linear semiflexible chains
- Monomers are in a bath at thermodynamic equilibrium.
- Monomers have positions and orientations.



Ordered growth of semiflexible filament

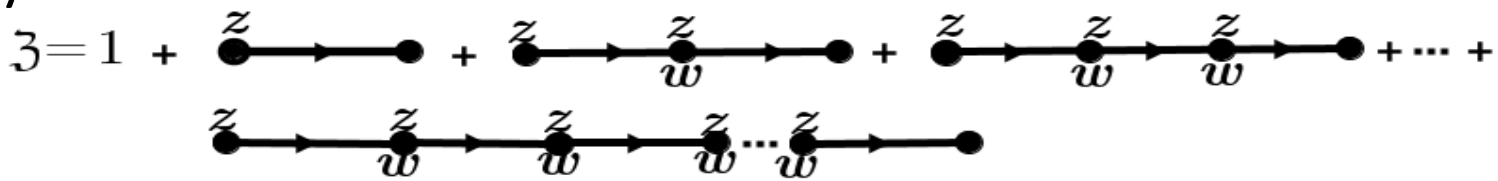
- The monomers' linkage to form the filament is controlled by a fugacity z.
- w Boltzman weight associated to the bending stiffness between bonds or monomers segments of the chain.

Grand canonical partition function for linear filaments

- The formalism consist of the definition of a grand canonical partition of the chain system and computation of average density profiles of the filament segments.
- It is a generating function that count all possible configurations of linear filaments that can be formed.

$$\Xi = \mathbf{1} + \sum_{N=1}^{\infty} \int \dots \int \boldsymbol{d^3 r_1 d^2 \hat{n}_1 d^3 r_2 d^2 \hat{n}_2 \dots d^3 r_N d^2 \hat{n}_N} \quad (2)$$
$$\boldsymbol{z(r_1, \hat{n}_1)\ w(r_1, \hat{n}_1, r_2, \hat{n}_2) z(r_2, \hat{n}_2) \dots w(r_{N-1}, \hat{n}_{N-1}, r_N, \hat{n}_N) z(r_N, \hat{n}_N)}$$

- Diagrammatically

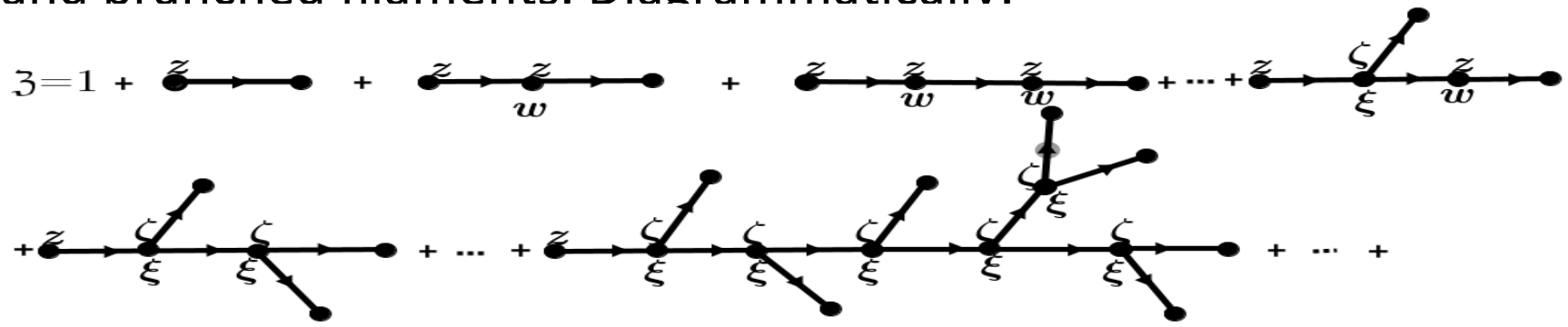


(3)

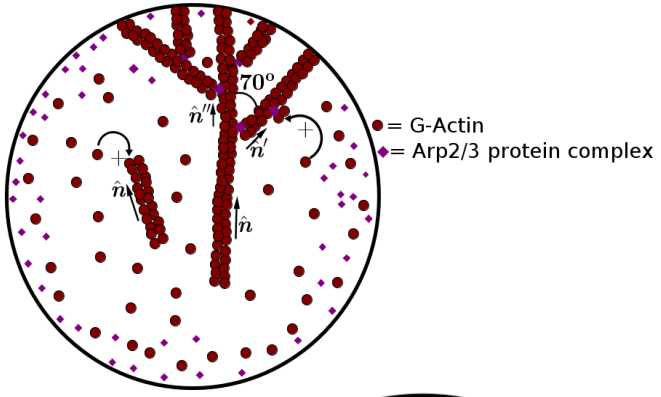
- Knowledge of average densities allows to predict the structure and conformation of the linear chains that are formed.
- Our main interest in this work is to be able to model and investigate physical properties of branching actin networks.

Extension of the monomer ensemble theory to confined branching actin networks

- **Model**: branching via Arp2/3 protein complex are now introduced to obtain a tree-like networks. (ζ, ξ) are (fugacity, Boltzmann weight) associated to branching points.
- The partition function count all possible conformations of linear and branched filaments. Diagrammatically:



(5) or



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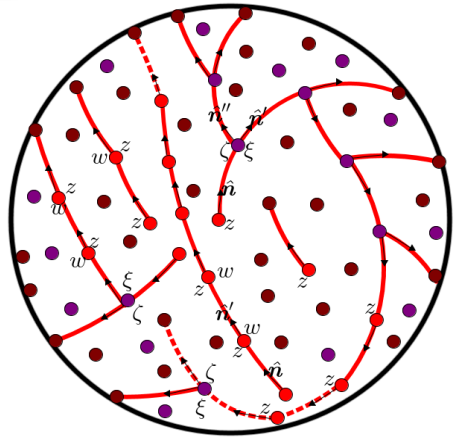
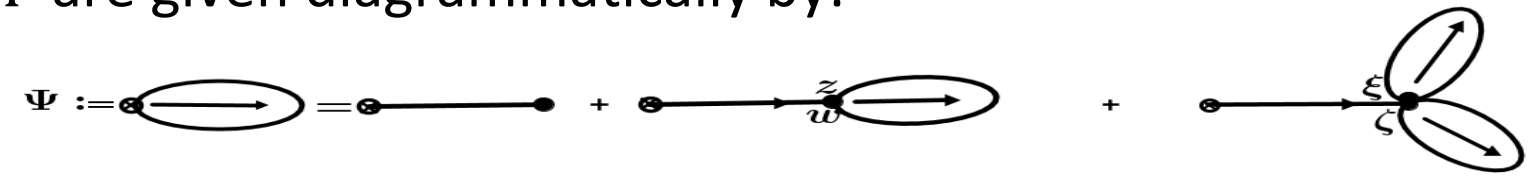


(6)

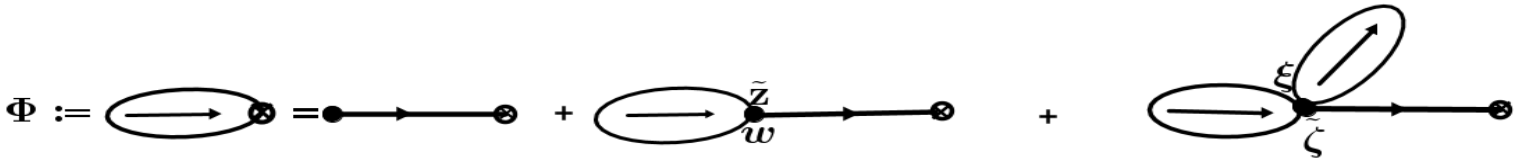
➢ We remark that $\mathfrak{Z}$ can be written in term of auxiliary function ψ or Φ as:

$$\mathfrak{Z} = \mathbf{1} + \int d^3\boldsymbol{r}\, d^2\hat{\boldsymbol{n}}\; z(\boldsymbol{r}, \hat{\boldsymbol{n}})\, \psi(\boldsymbol{r}, \hat{\boldsymbol{n}}) \quad (5) \qquad \text{or} \qquad \mathfrak{Z} = \mathbf{1} + \int d^3\boldsymbol{r}\, d^2\hat{\boldsymbol{n}}\, \tilde{z}(\boldsymbol{r}, \hat{\boldsymbol{n}})\, \Phi(\boldsymbol{r}, \hat{\boldsymbol{n}}) \quad (6)$$

where ψ or Φ are given diagrammatically by:



(7)



(8)

➢ or in term of integral equation:

$$\Psi(\boldsymbol{r},\hat{\boldsymbol{n}}) = 1 + \int_{\boldsymbol{r},\hat{\boldsymbol{n}}} \mathrm{d}^3\boldsymbol{r}'\mathrm{d}^2\hat{\boldsymbol{n}}' w(\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}') z(\boldsymbol{r},\hat{\boldsymbol{n}}')\Psi(\boldsymbol{r},\hat{\boldsymbol{n}}') + \int_{\boldsymbol{r}',\hat{\boldsymbol{n}}',\boldsymbol{r}'',\hat{\boldsymbol{n}}''} \mathrm{d}^3\boldsymbol{r}'\mathrm{d}^2\hat{\boldsymbol{n}}'\mathrm{d}^3\boldsymbol{r}''\mathrm{d}^2\hat{\boldsymbol{n}}''\xi(\boldsymbol{r},\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}',\hat{\boldsymbol{n}}'')\zeta(\boldsymbol{r},\hat{\boldsymbol{n}}',\hat{\boldsymbol{n}}'')\Psi(\mathrm{r}',\hat{\boldsymbol{n}}')\Psi(\boldsymbol{r}'',\hat{\boldsymbol{n}}'') \quad (9)$$

and

$$\Phi(\boldsymbol{r},\hat{\boldsymbol{n}}) = 1 + \int_{\boldsymbol{r},\hat{\boldsymbol{n}}} \mathrm{d}^3\boldsymbol{r}'\mathrm{d}^2\hat{\boldsymbol{n}}' \tilde{z}(\boldsymbol{r},\hat{\boldsymbol{n}}') w(\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}')\Psi(\mathrm{r},\hat{\boldsymbol{n}}') + \int_{\boldsymbol{r}',\hat{\boldsymbol{n}}',\boldsymbol{r}'',\hat{\boldsymbol{n}}''} \mathrm{d}^3\boldsymbol{r}'\mathrm{d}^2\hat{\boldsymbol{n}}'\mathrm{d}^3\boldsymbol{r}''\mathrm{d}^2\hat{\boldsymbol{n}}''\xi(\boldsymbol{r},\hat{\boldsymbol{n}},\boldsymbol{n}',\boldsymbol{n}'')\tilde{\zeta}(\boldsymbol{r},\boldsymbol{n}',\hat{\boldsymbol{n}}'')\Psi(\boldsymbol{r}',\boldsymbol{n}')\Phi(\boldsymbol{r}'',\hat{\boldsymbol{n}}'') \quad (10)$$

Confinement

- Choice of z and ζ allows to solve the non-linear coupled integral equations of ψ and Φ.

$$z(\boldsymbol{r},\hat{n}) = z_0\theta(\boldsymbol{r},\hat{n}) \quad \text{and} \quad \tilde{z}(\boldsymbol{r},\hat{n}) = z_0\theta(\boldsymbol{r},-\hat{n}) \quad \text{where} \quad \theta(\boldsymbol{r},\hat{\boldsymbol{n}}) = z_0 \times \begin{cases} 1, & \text{if } \boldsymbol{r} \in \mathbb{L} \text{ and } \boldsymbol{r}+\ell\hat{\boldsymbol{n}} \in \mathbb{L} \\ 0, & \text{otherwise} \end{cases} \tag{11}$$

$$\zeta(r,\hat{\boldsymbol{n}}_1,\hat{\boldsymbol{n}}_2) = \zeta_0 \times \begin{cases} 1, & \text{if } \boldsymbol{r} \in \mathbb{L} \text{ and } \boldsymbol{r}+\ell\hat{\boldsymbol{n}}_1 \in \mathbb{L} \\ \text{and} & r+\ell\hat{\boldsymbol{n}}_2 \in \mathbb{L} \\ 0, & \text{otherwise} \end{cases} \tag{12}$$

- Choice of the Boltzmann weights ξ and *w*:

$$w(\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}') = \frac{w_0}{\mathcal{N}_w} e^{\beta\epsilon\,\hat{\boldsymbol{n}}\cdot\hat{\boldsymbol{n}}'}. \tag{14}$$

where

$$\mathcal{N}_w = \sum_{\hat{\boldsymbol{n}}'} w(\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}')$$

(13)

$$\xi(\boldsymbol{r},\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}',\hat{\boldsymbol{n}}'') = \frac{\mathcal{N}_w}{\mathcal{N}_\xi} w(\hat{\boldsymbol{n}},\hat{\boldsymbol{n}}') \times e^{\left(-\xi_0\left(\hat{\boldsymbol{n}}\cdot\hat{\boldsymbol{n}}''-\cos\alpha\right)^2-\xi_1\left(\hat{\boldsymbol{n}}'\cdot\hat{\boldsymbol{n}}''-\cos\alpha\right)^2\right)}.$$

- The persistence length of actin filaments is expressed in term of bending stiffness.

- ψ and Φ are computed numerically on the lattice.

Average densities and order parameter fields

- Total average density of segments is

$$\rho(\boldsymbol{r}, \hat{\boldsymbol{n}}) = \rho_z(\boldsymbol{r}, \hat{\boldsymbol{n}}) + 2\,\rho_\zeta(\boldsymbol{r}, \hat{\boldsymbol{n}}) \qquad (15)$$

where

$$\rho_z(\boldsymbol{r}, \hat{\boldsymbol{n}}) = \frac{z(\boldsymbol{r}, \hat{\boldsymbol{n}})}{3}\frac{\delta 3}{\delta z(\boldsymbol{r}, \hat{\boldsymbol{n}})} = \frac{z(\boldsymbol{r}, \hat{\boldsymbol{n}})}{3}\psi(\boldsymbol{r}, \hat{\boldsymbol{n}})\Phi(\boldsymbol{r}, \hat{\boldsymbol{n}})$$

density of segments not involved in branching points

$$\rho_\zeta(\boldsymbol{r}, \hat{\boldsymbol{n}}) = \frac{\zeta(\boldsymbol{r}, \hat{\boldsymbol{n}}, \hat{\boldsymbol{n}}', \hat{\boldsymbol{n}}'')}{3}\psi(\boldsymbol{r}, \hat{\boldsymbol{n}}')\Phi(\boldsymbol{r}, \hat{\boldsymbol{n}})\psi(\boldsymbol{r}, \hat{\boldsymbol{n}}'')$$

density of branching points.

- Degree of polymerization or mean number of segments inside the confining region

$$< N > = \sum_{\boldsymbol{r}} \rho(\boldsymbol{r}) \qquad (16)$$

where

$$\rho(\boldsymbol{r}) = \sum_{\hat{\boldsymbol{n}}} \rho(\boldsymbol{r}, \hat{\boldsymbol{n}})$$

- Orientational order parameter field

$$Q(\boldsymbol{r}) = \sum_{\hat{\boldsymbol{n}}} \frac{1}{2}(1 - 3(\hat{\boldsymbol{n}}.\hat{\boldsymbol{u}})^2)\rho(\boldsymbol{r}, \hat{\boldsymbol{n}}) \qquad (17)$$

for 3*D* networks and

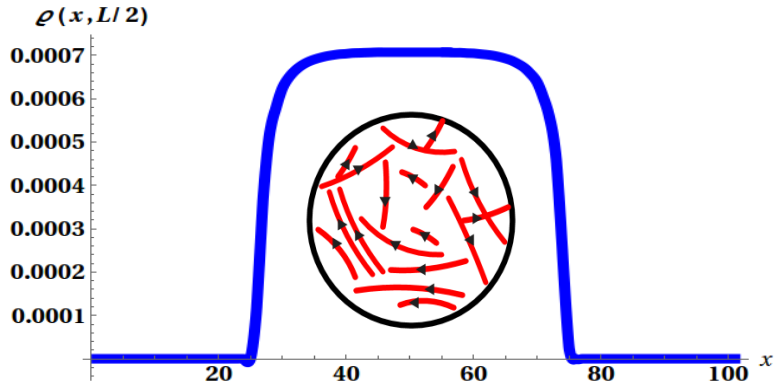
$$Q(\boldsymbol{r}) = \sum_{\hat{\boldsymbol{n}}} (1 - 2(\hat{\boldsymbol{n}}.\hat{\boldsymbol{u}})^2)\rho(\boldsymbol{r}, \hat{\boldsymbol{n}}) \qquad (18)$$

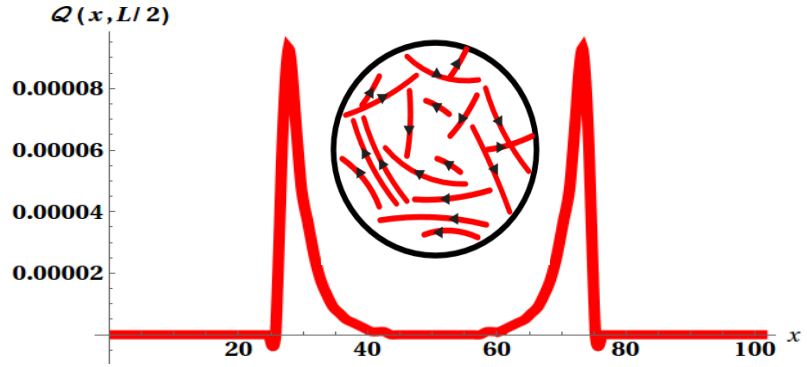
for 2D

- If $Q(\boldsymbol{r}) > 0$, filaments or segments of the networks are aligned parallel to the cell membrane or wall.
- If $Q(\boldsymbol{r}) < 0$, filaments are aligned radially or perpendicular to it.
- If $Q(\boldsymbol{r}) = 0$, are isotopically distributed in the confining cell domain.

Numerical results

- By varying z_o and ζ_o, 3types of 2D and 3D actin networks are obtained.
- The persistence length ℓ_p of actin filaments is about 17.7μm.
- The networks is confined in a spherical rigid cell of diameter *D,* the ratio ℓ_p/D~1.2, $\varepsilon = \frac{8.15}{k_B T}$, $\xi_0 = 1$
- $(1 - z_o)^2 \geq 4\,\zeta_o$ represent the unconfined limit or domain of validity of our model.
- Density (blue graphs) and order field (red graphs) profiles through the centre of the spherical cell.

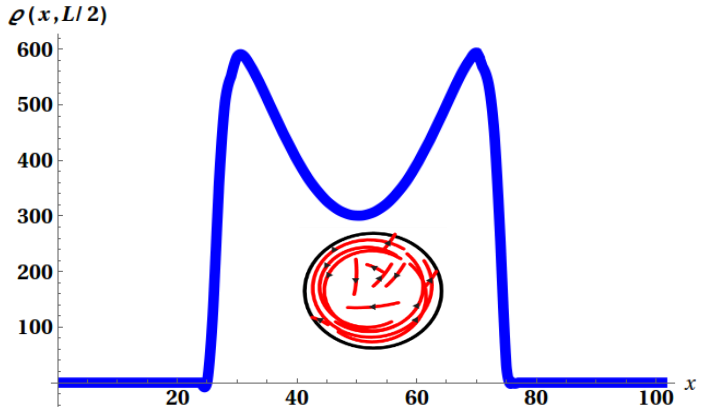


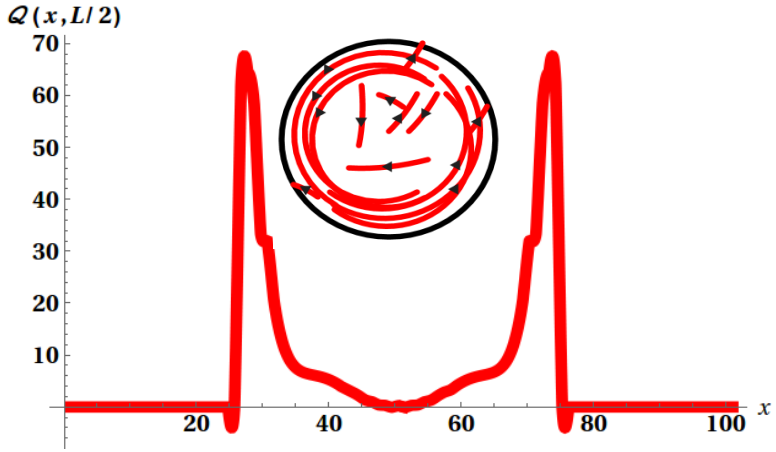


z_o=0.5, ζ_o=0.001, $< N > < D$, networks dominated by shorts filaments. Convex-shaped density distribution distributed with preference of parallel alignment near the wall, isotropically distributed in the middle.

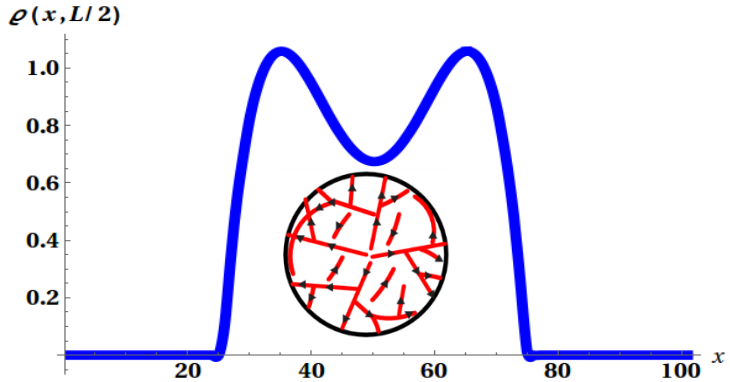
Density and order field profiles

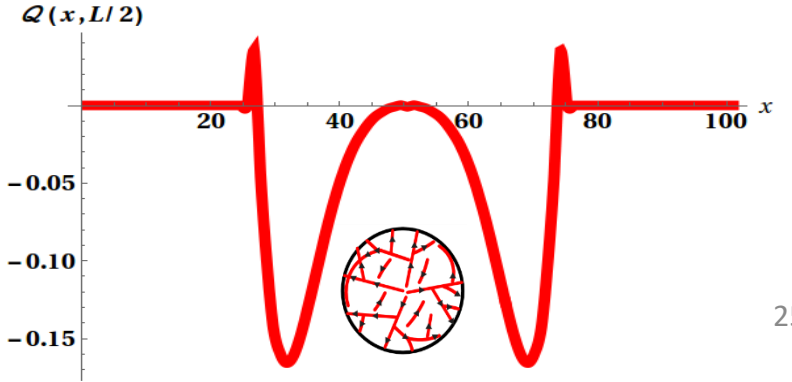
- z_o=0.75, ζ_o=0.001, $L > D$, networks dominated by long linear filaments. Concave-shaped distribution of segment with parallel alignment near the cell membrane and isotropic in the middle.



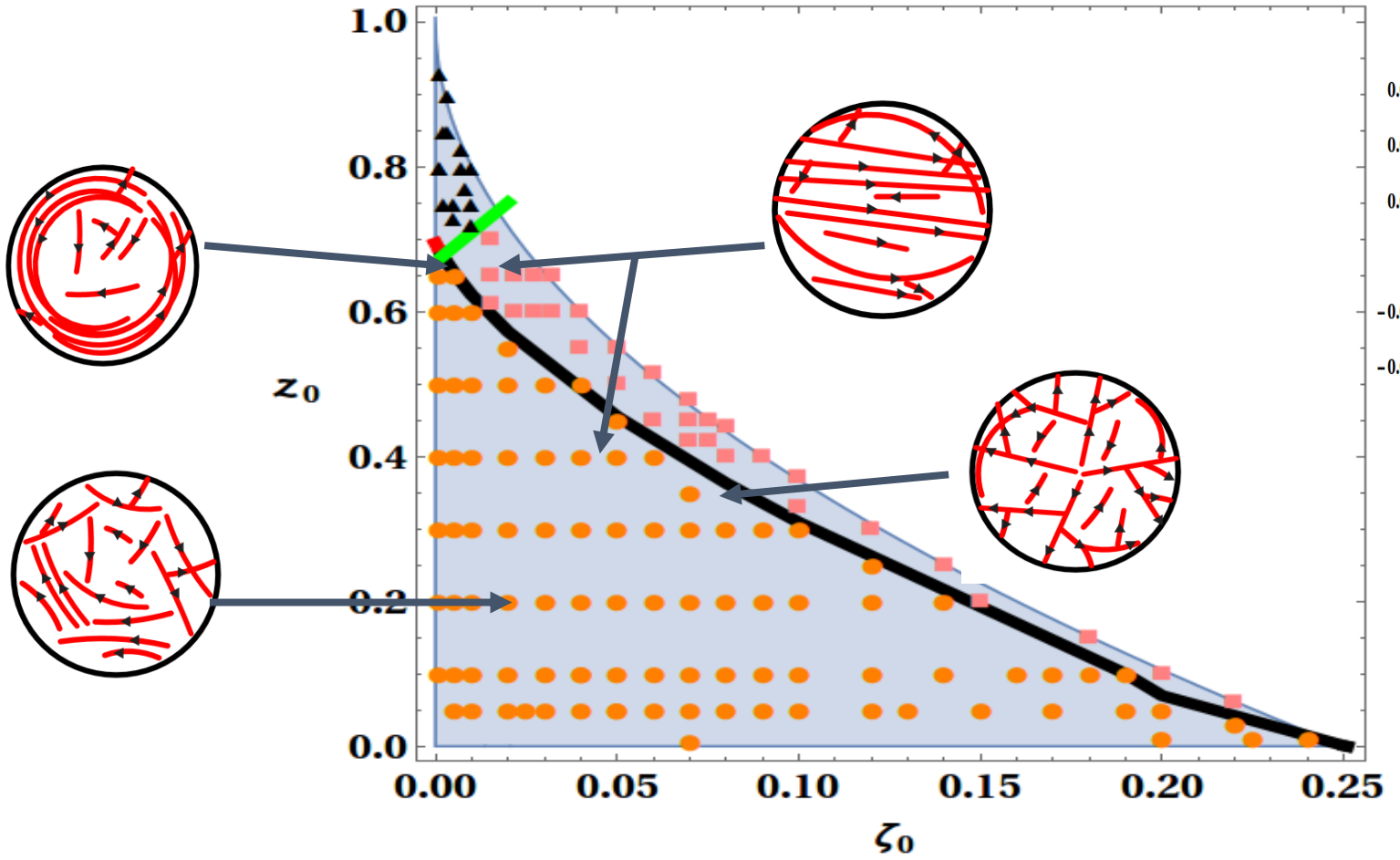


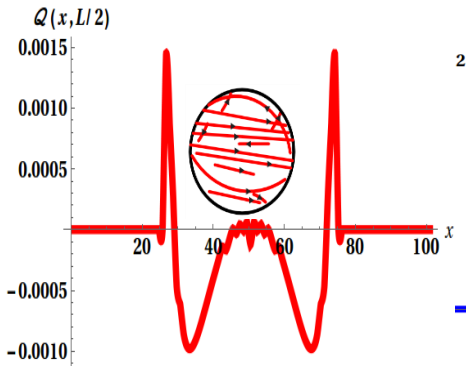
- z_o=0.516, ζ_o=0.06, Branched networks. Concave-shaped distribution of segment with perpendicular alignment near the cell membrane and isotropic in the middle.

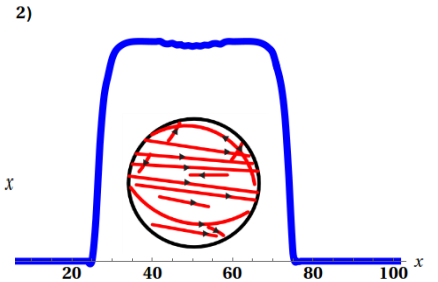




Phase diagram





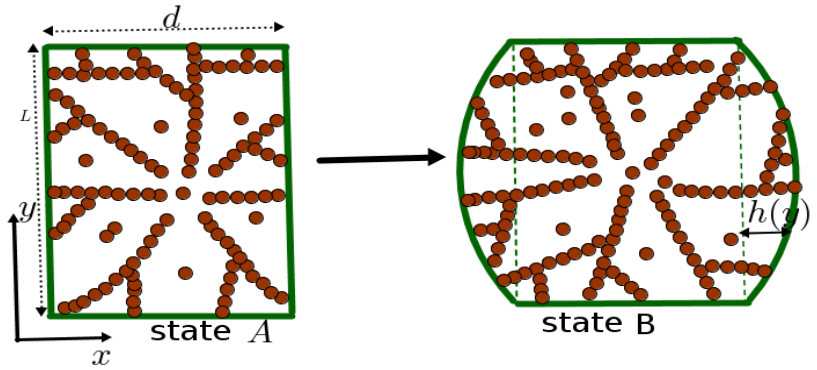


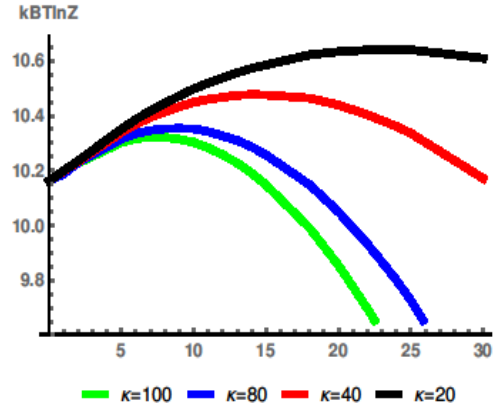
- z_o=0.69, ζ_o=0.001, $L \sim D$, networks of filaments with length comparable to the size of the confining regions.

[1]Azote S. and Müller-Nedebock K.K., Density fields for branching, stiff networks in rigid confining regions , Eur. Phys. J. E (2019) 42: 23. https://doi.org/10.1140/epje/i2019 - 11784-0.

From Structure to cell mechanics: network under compression

- Is the volume of the cell conserved under compression or stretching forces? (the membrane of the 2d cell can bend in the direction *x*.)

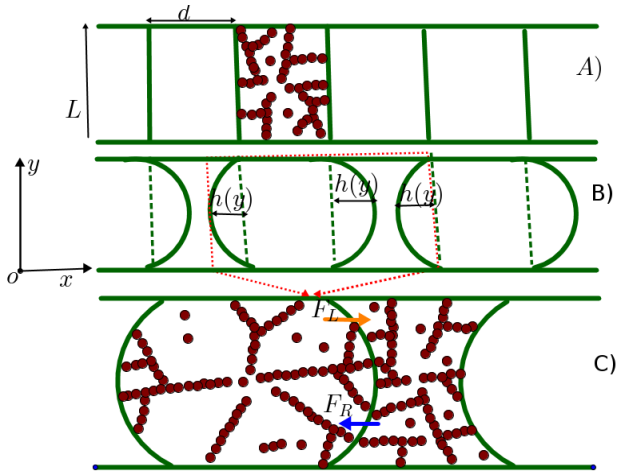




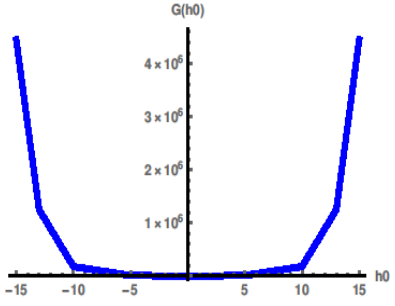
ℓ_p/L~1.2

z_o=0.5, ζ_o=0.06

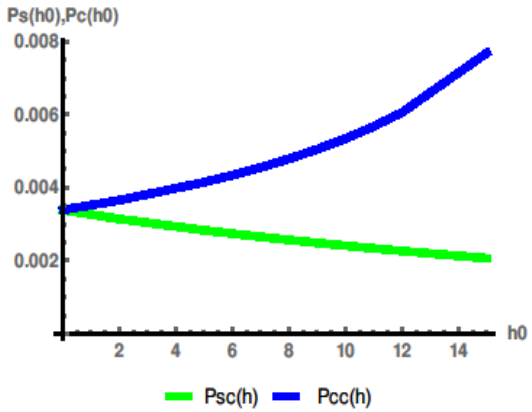
- Stability of the cells against compression:



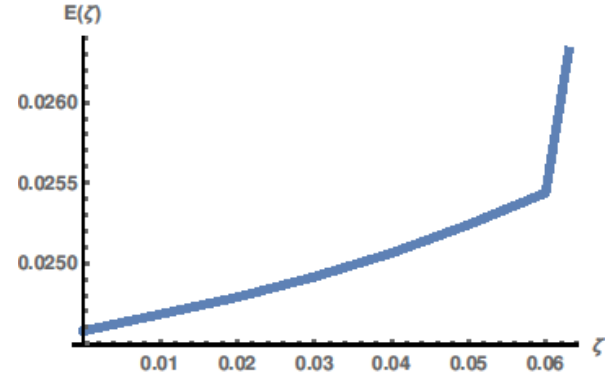
$$G(h_0) = \mu < N(h_0) >$$



Gibbs free energy



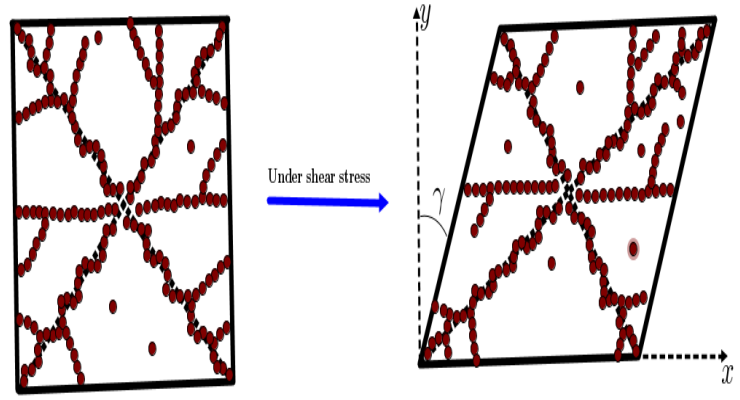
Pressure balance between left and right cells (C)



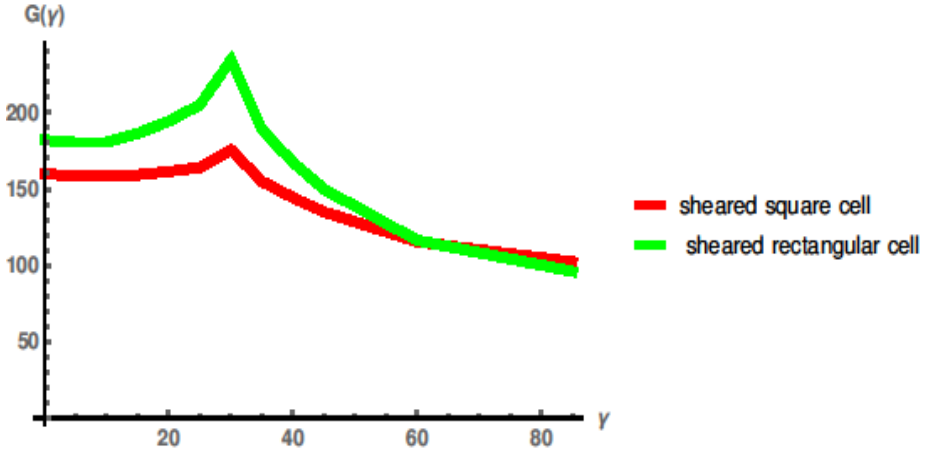
The Young modulus increases as the stiffness of the network increases

stability against shear

- Are our tissue cells stable against shear?



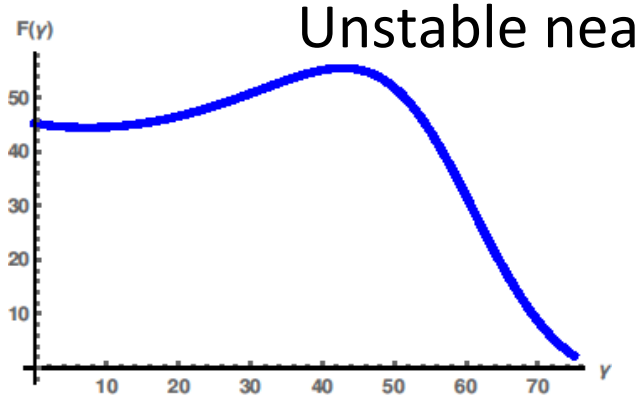
- Numerical results



Gibbs free energy. Unstable near a critical angle $\pi/6$.

- Analytical results

Unstable near a critical angle



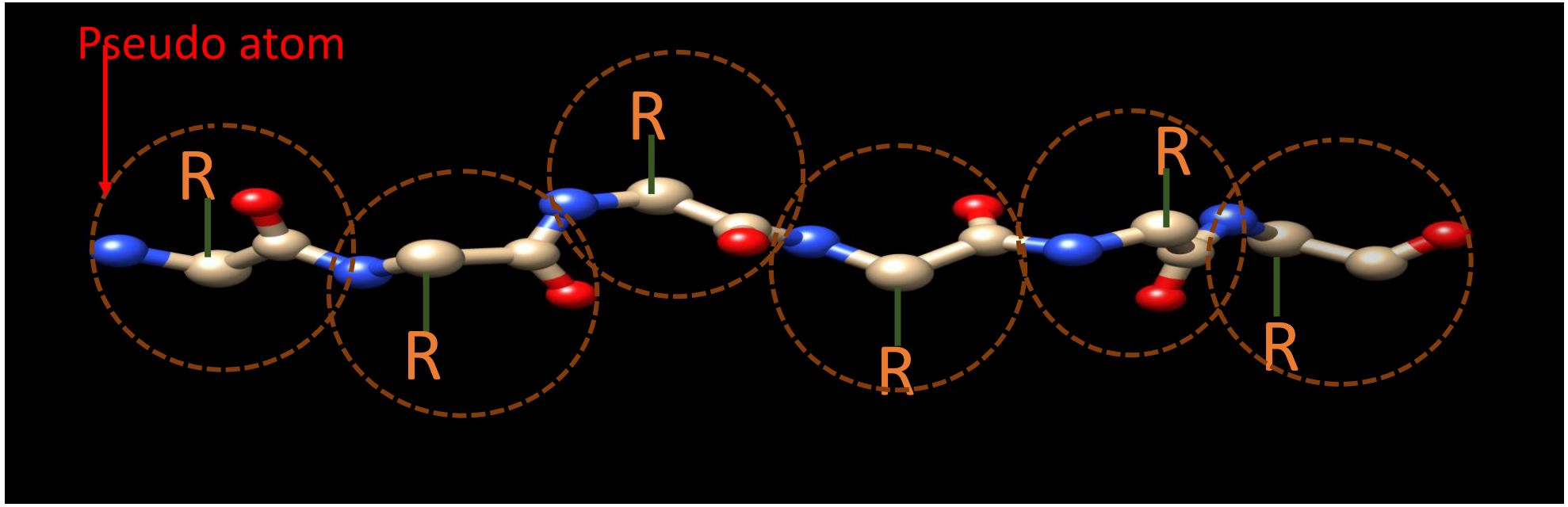
$\pi/4$

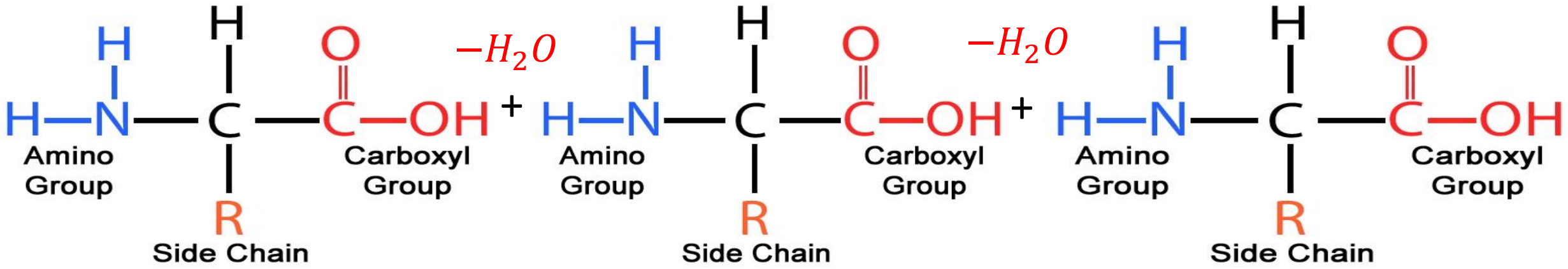
- We conclude that γ Is between $\pi/6$ and $\pi/4$.

- The instability may be due the fact that either shear favour the network growth along one diagonal against the other or to the buckling instability.

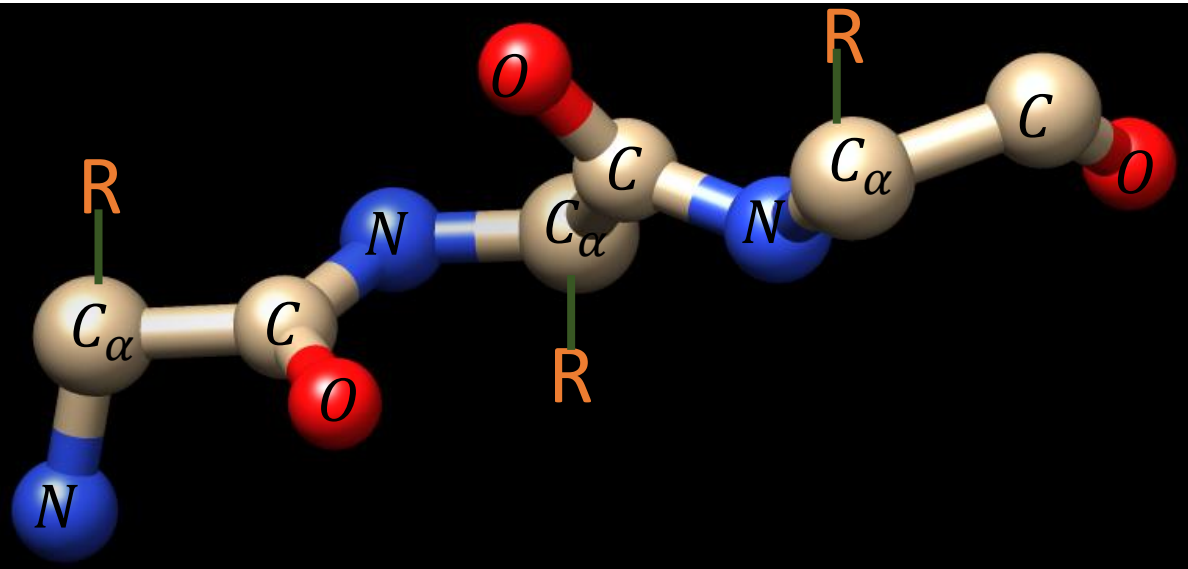
Coarse grained modelling of DNA and proteins

- **coarse-grained models** are used to simulate the behavior of complex systems using their (simplified) representation.
- Many coarse-grained models have been proposed and each used for computational modeling of specific molecules: nucleic acid (DNA,RNA), proteins, membrane, lipid.
- An example of coarse-grained representation of a short protein (peptide):



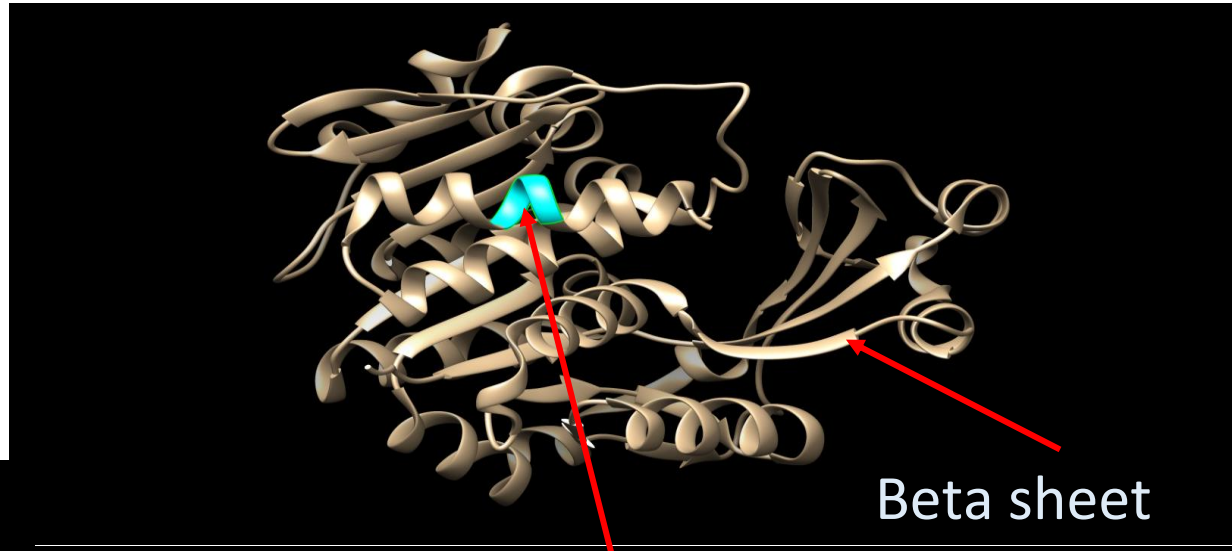

$-H_2O$
$-H_2O$
Amino Group
Carboxyl Group
Side Chain
Amino Group
Carboxyl Group
Side Chain
Amino Group
Carboxyl Group
Side Chain

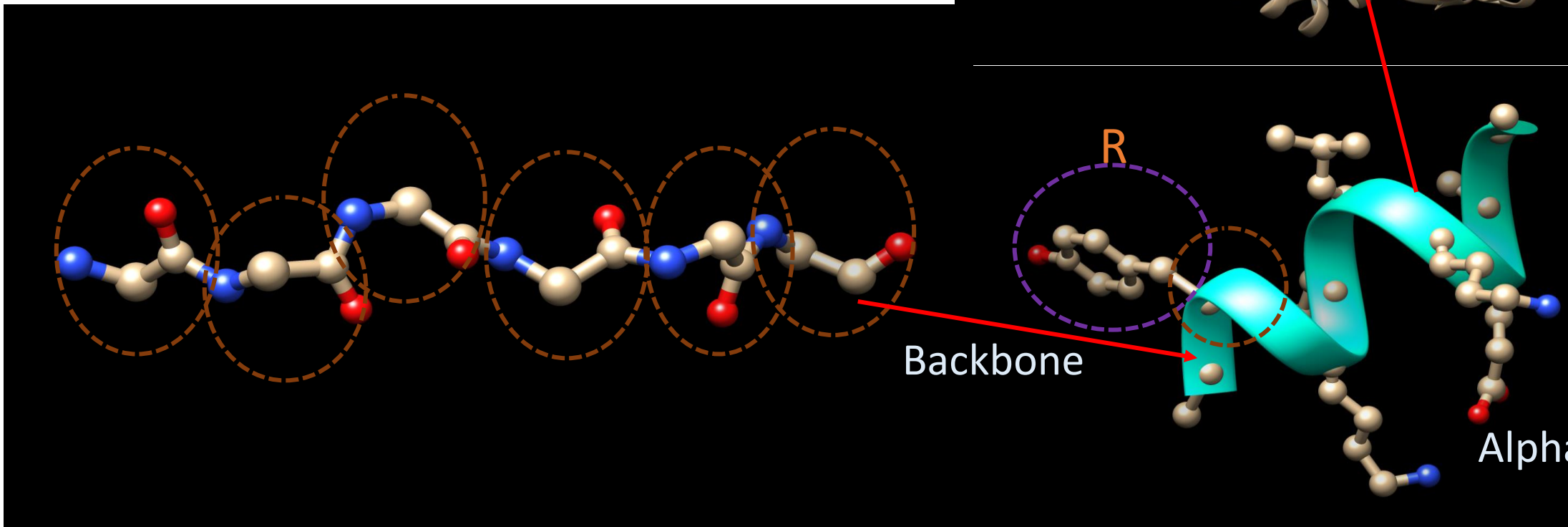
peptide


R
C_α
C
O
N
N
C_α
C
O
R
R
C_α
C
O
N

AIM

- Study the real protein folding
- Protein fold into specific secondary structure to function





About protein Folding

- Protein folding is one of the topics investigated in my group

Home > The Journal of Chemical Physics > Volume 151, Issue 17 > 10.1063/1.5123720

PREV NEXT

No Access . Published Online: 01 November 2019 Accepted: October 2019

Chain stiffness bridges conventional polymer and bio-molecular phases

J. Chem. Phys. **151**, 174901 (2019); https://doi.org/10.1063/1.5123720

Tatjana Škrbić[1,2,a)], Jayanth R. Banavar[1,b)], *and* Achille Giacometti[2,3,c)]

Proteins. 2019 Mar;87(3):176-184. doi: 10.1002/prot.25619. Epub 2018 Nov 18.

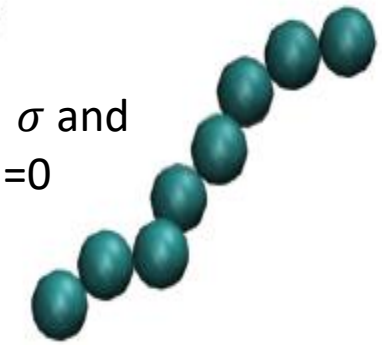
The elixir phase of chain molecules

Tatjana Škrbić [1] [2], Trinh X Hoang [3], Amos Maritan [4], Jayanth R Banavar [2], Achille Giacometti [1]

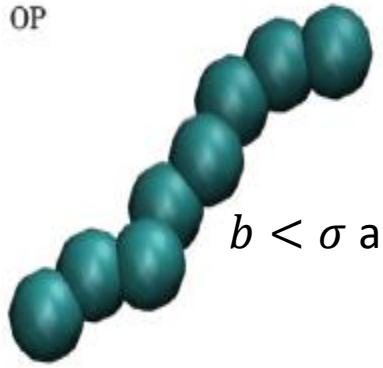
Affiliations + expand

PMID: 30371948 DOI: 10.1002/prot.25619

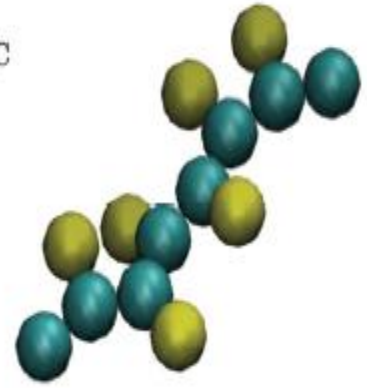
➢ Models (images are from ref. of previous slide)



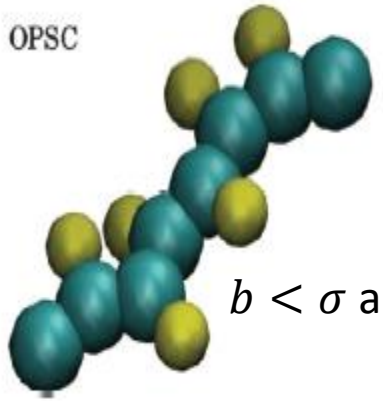
$b \approx \sigma$ and
σ_{sc} =0



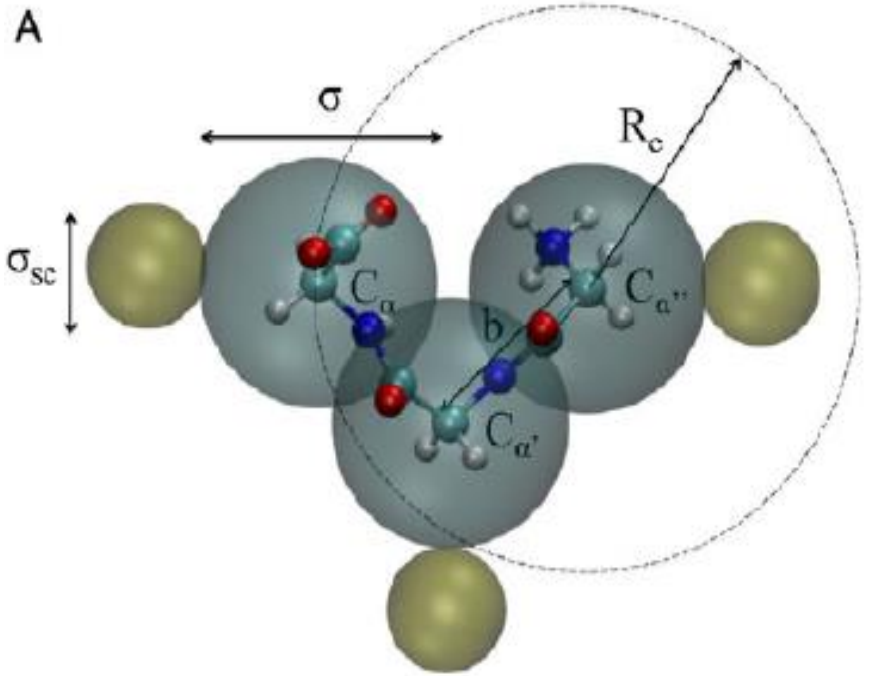
$b < \sigma$ and σ_{sc} =0



$b \approx \sigma$ and σ_{sc} >0



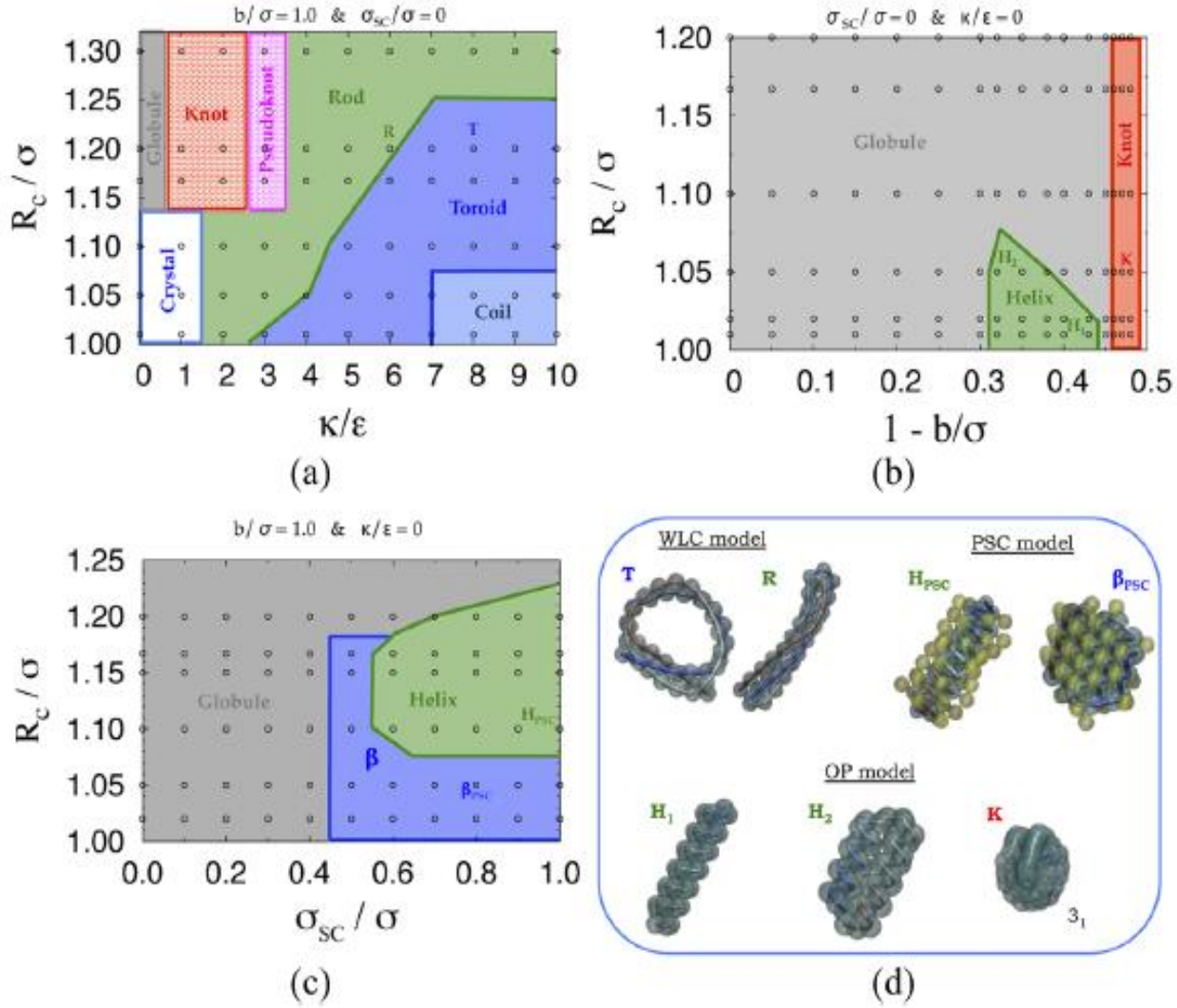
$b < \sigma$ and σ_{sc} >0



➢ Coarse grained modelling is all about defining a correct force fields for the model

$$\phi(r) = \begin{cases} +\infty, & r < \sigma \\ -\varepsilon, & \sigma < r < R_c \equiv \lambda\sigma \\ 0, & r > \lambda\sigma \end{cases}$$

➢Results from papers above and insights



Ground state phase diagram with wide range of ground state conformations, including a coil, a globule, a toroid, rods, helices, and zig-zag strands resembling *β*-sheets, as well as knotted conformations

About DNA

- Investigate also a class of biological polymer, the nucleic acids (DNA and RNA)
- coarse-grained nucleotide-level representation using the **oxDNA** model
- Allows extract thermodynamic, dynamic and structural information in details
- Mechanical and structural properties can be investigated for objects as large as a full-scale DNA origami .

oxDNA model: Force fields

- Interaction U in oxDNA for the DNA model (by T. E. Ouldridge et al, 2011)

$$U = \sum_{nn} \left(U_b + U_s + U_{\text{exc\_backb}}\right) + \sum_{\text{others}} \left(U_{\text{HB}} + U_{\text{cross\_stack}} + U_{\text{exc\_b}ases} + U_{\text{coaxial\_stack}}\right)$$

- constructed using FENE spring, LJ, Morse, Harmonic potential, modulation and truncation potentials (by T. E. Ouldridge et al, 2011).

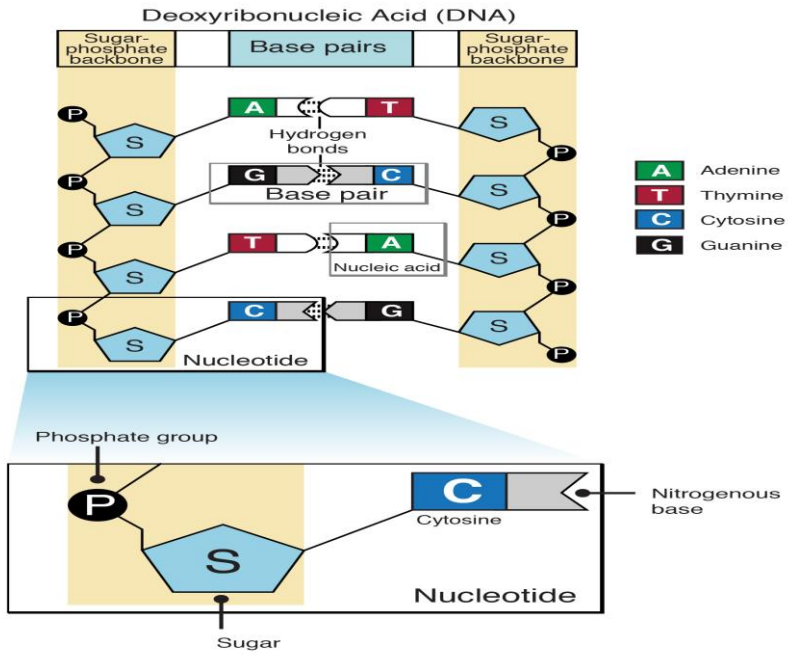
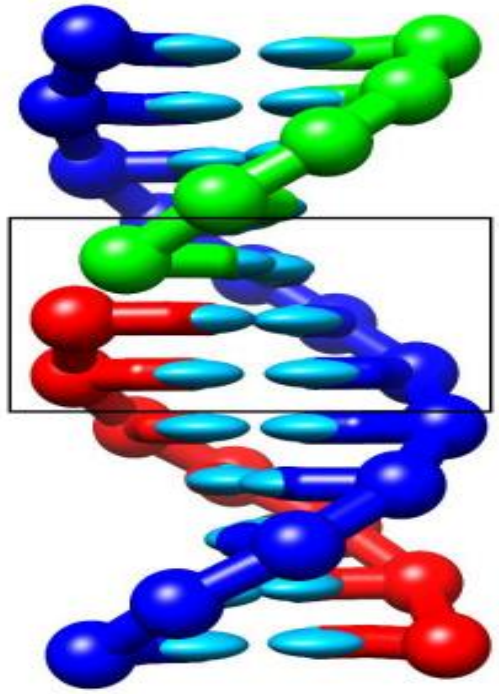
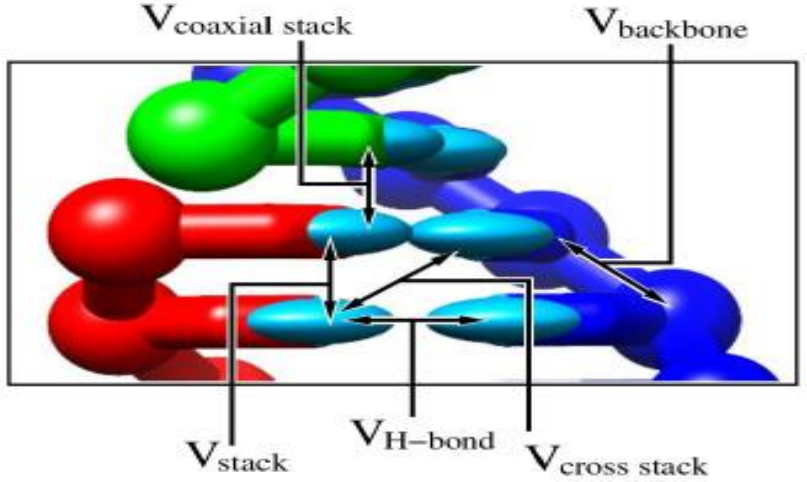


Image taken online





Some results using oxDNA model

Home > The Journal of Chemical Physics > Volume 138, Issue 8 > 10.1063/1.4792252

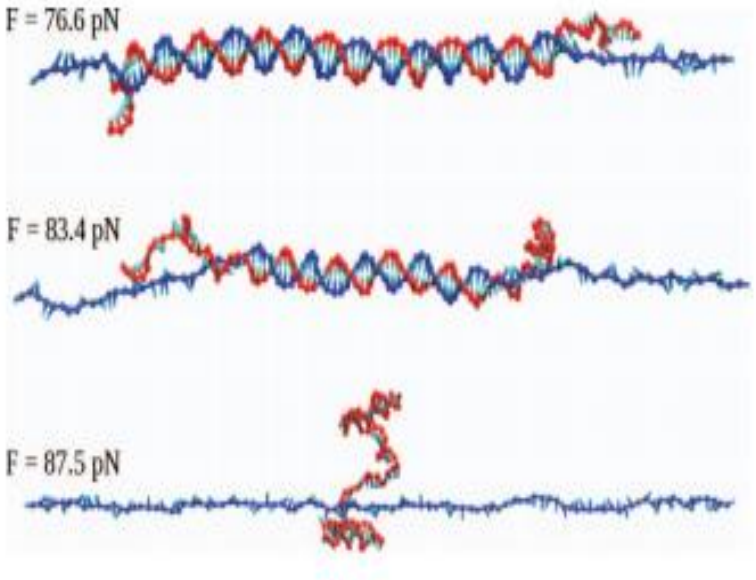
No Access . Published Online: 22 February 2013 Accepted: January 2013

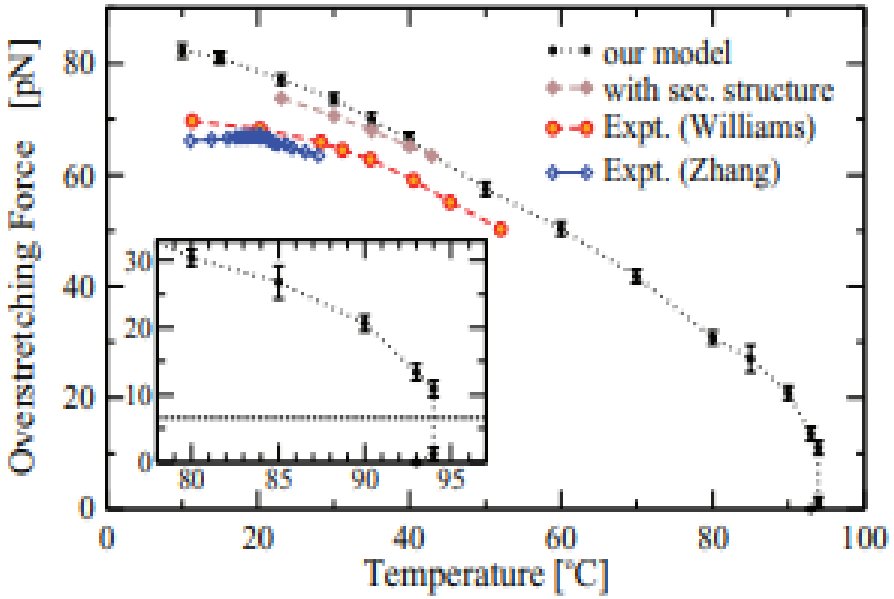
Coarse-grained simulations of DNA overstretching

J. Chem. Phys. **138**, 085101 (2013); https://doi.org/10.1063/1.4792252

Flavio Romano[1], Debayan Chakraborty[1, a)], Jonathan P. K. Doye[1, b)], Thomas E. Ouldridge[2], *and* Ard A. Louis[2]

- The model reproduces the temperature dependence of the overstretching force well





Extending OxDNA Model to model Proteins

- Model the backbone and side chain in more detailed way
- Define the suitable force fields in oxDNA to model proteins and also protein-DNA interactions
- oxDNA enable MD and Monte Carlo simulations
- Preliminary results are promising and hope to show them very soon

Conclusions

- We have formulated a model for branching actin cytoskeletal networks confined in cell with any geometry. properties.

- We have shown that these properties allows the branched networks to ensure the stability of tissue cells under compression.

- Equilibrium numerical calculations give us interesting phase diagram of actin networks enabling us to make predictions of the networks structural and conformational

- We have shown using simple cell geometries that, tissue cells can not be sheared indefinitely.

- Our model is being tested experimentally.

- Our results can be used as basis to explore non equilibrium behaviour of branching actin networks in cells.

- Our findings are of relevance in medicine as well as in biotechnological or industrial applications:
  - Knowledge about the structures and conformations of these networks is important for the diagnosis of the sick cells.
  - This can also help in conception of artificial cells.

- We have also introduced the coarse-grained modelling of DNA and proteins, very useful in cell biology, medicine nanotechnology, and industry

- We have also introduced the coarse-grained modelling of DNA and proteins, very useful in cell biology, medicine nanotechnology, and industry

Acknowledgement

- **I am grateful to OWSD, SIDA and NRF who have funded my PhD work.**
- **Thanks to ASP for his support**
- **To all my Supervisors, Mentors and friends**
- **I also would like to thank all my group members here at Ca Foscari University**





Thank you all for your attention ☺!

Any question?