# Bacterial Chromosome Organization: crosslinks, confinement and crowders play the pivotal roles.

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# Acknowledgments

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CC: Tung Le, .. Laub, Science (2013)
*E. coli*: Caglieri et.al., NAR (2013).

Ph.D. student: **Tejal Agarwal.**

FUNDING: DST-India, DBT-India.

# DNA: Basic facts.

Human DNA has $6.4 \times 10^9$ base pairs.

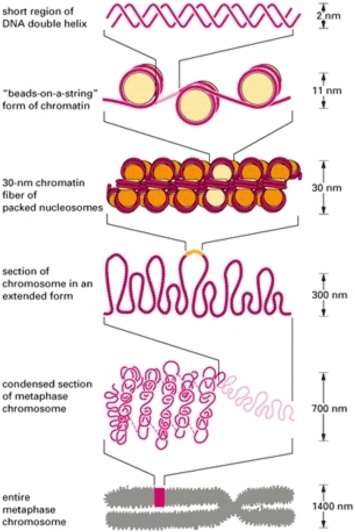
Length $2m$ packed in nucleus $\sim (10\mu)^3$.

**Some imp numbers:**

**Base pair : 3.3Å.**

**Helix pitch =3.4 nm OR 10.4 BP.**
**Chain width $\sim$ 2nm.**

**Kuhn Segment: 300 BP or 100nm.**

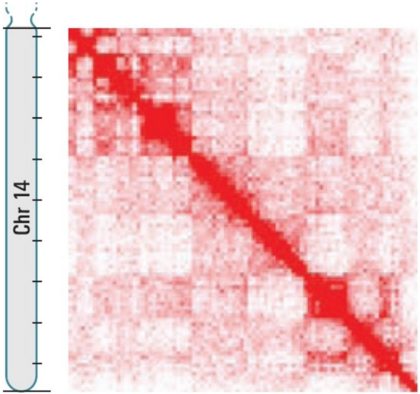


**DNA packed in nucleus by organizing into hierarchy of Mesoscale structures.**

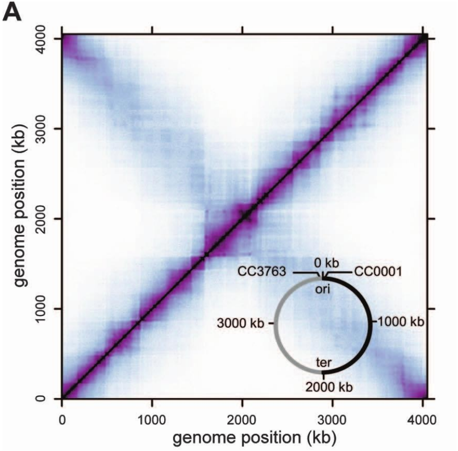
# Single Chromosome: Chromosmal Contact Maps.

## Single chromosome is not organized Randomly: TADs

Lieberman-Aiden.., Science, (2009):HUMAN



Le, Laub, Science (2013) *C.Crescentus*



**Higher probabilities to find certain segments of chain in contact with specific other segments. How is the organization achieved?**

# What causes large scale organization of DNA?

- **Can we predict the 3d organization of DNA?: Experimentally verify.**
*Mirny (MIT), Marenduzzo (UK), Nicodemi (Italy), Joyeux (France), Mulder-Debashish (Netherlands-India)*

## Our Primary Observation:

- Cross-links at **specific** points along the chain leads to the organization of the DNA-polymer ?! - DNA binding proteins.

- **Position of cross-link (CL) chosen from the Contact Map.**

**DNA segments with highest probability of contact were cross-linked together in a bead-spring model of ring polymer.**

- Random cross-links: Nature of organization is different.
More *diffuse* organization. 10 different CL sets.

# Primary Results:

**Bead spring ring polymer model of bacterial DNA**.

*E. coli*: 4.642 million **Base Pairs** : **4642** monomers :: 1 monomer ≡ 1000 BP.
*C. Crescentus*: 4.017 million **Base Pairs** : **4017** monomers.

- *E. coli*: 82 cross-links at specific positions along contour → organization.
  **38** CLs in confinement.

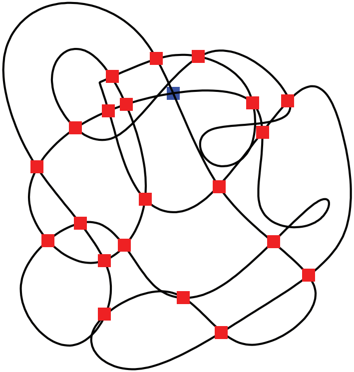
- *C. crescentus*: 60 cross-links in DNA → organization.
  **33** CLs in confinement.

Publications: Tejal Agarwal, G.P. Manjunath, F. Habib, **A.C.**

J.Phys: Condens. Matter (2018); Europhys. Lett. (2018)
Submitted as Part-1,2 to J.Chem.Phys: arXiv:1808.09400; arXiv:1808.09396.

# Modelling-1: Choose Bacteria with single DNA.

1. *E. coli.* 4.642 million base pairs = 4642 monomers.
   *CC* 4 million BPs: 4017 monomers.
2. 1 coarse grained monomer in model = 1000 BP.
3. Bead spring model of polymer.
4. Persistence length of DNA : $\ell_p \equiv 150$ BP $\equiv 50$ nm
5. RING polymer.
6. Ex. Volume radius $= 0.2b$: Suitably truncated Lennard Jones interactions.

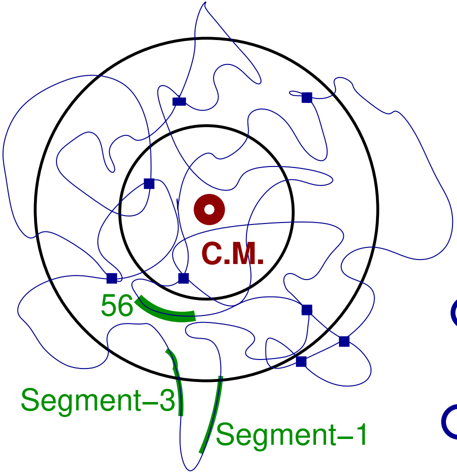


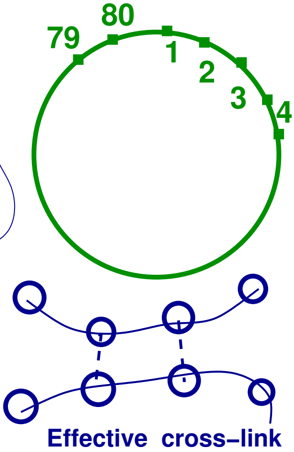
**Cross-link between monomers A, B modelled by $V_{AB}(r) = \kappa_b(r_{AB} - b)^2$**

**How can we say that a polymer is structured/organized ?**

# Quantities determining Structure ?? $R_g$..and..

CL: CROSS LINKs





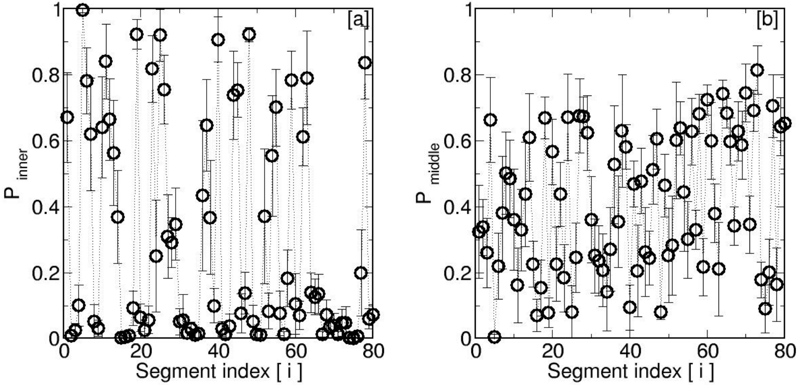
**E. coli : 4642 monomers: 80 segments of 58 monomers each.**

**Calculate positional corr. of segments.**

- **Distance from center of Mass**
- **Angular correlations.**

# Spatial location of a Ecoli segment: Inner/ Middle/ Outer?

**Calculate $R_g$;** • **$R_g$ (Random CLs) $<$ $R_g$ (Bio CLs): Same no. of CLs**



S. Karlin et.al, J. of Bacter., **183**, 5025(2001).
List: 47/4000 most expressed Genes

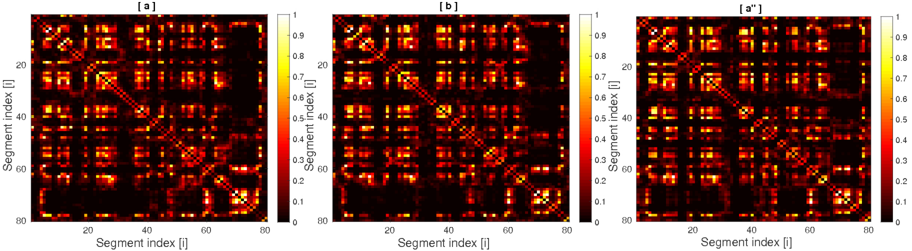
**82 effective CLs**

**37 out 47 genes are in peripheral regions.**

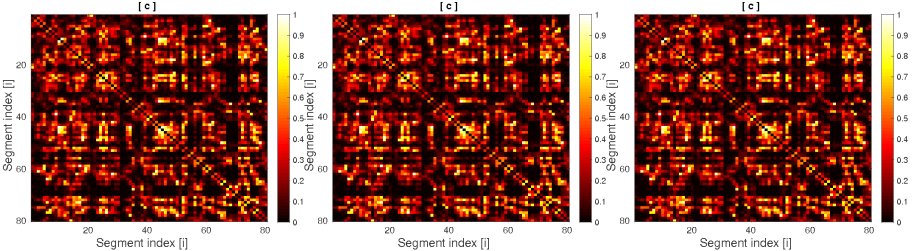
- **Well defined location of CLs/segments.**

# Positional correlation of segments: (without confinement).

Ecoli ≡ 82 CLs: Comparison from 3 independent runs:



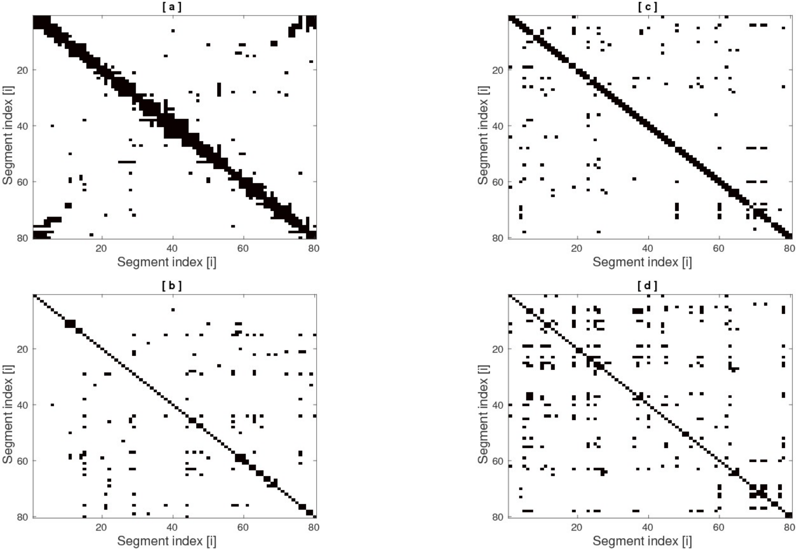
82 CLs at **Random** locations along chain: BUT



**Fewer cross-links: The pattern/correlation is lost.**

# Compare EXP & SIM: Coarse-grained maps: Highest Prob.

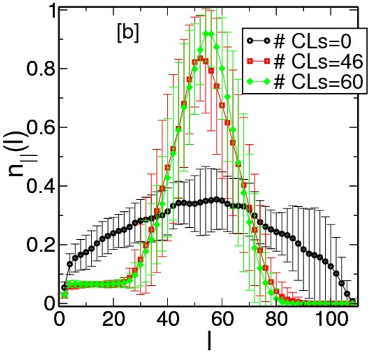
*C. crescentus (EXP)*　　　　*E. coli (EXP)*



*SIM.*

- **Simulations and exp match for E. coli but partially for CC.**

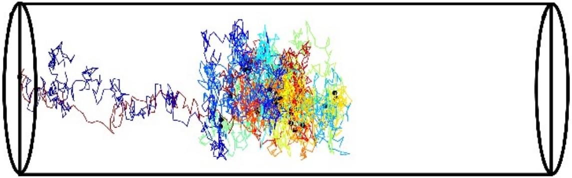
# CC-DNA confined in cylinder, Aspect Ratio 1:7.5



49 CLs: 26 effective CLs.
60 CLs: 33 effective CLs.

**Cyl. Radius=7a, Axis: 108a**

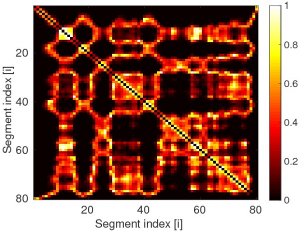
**Monomer-1 (ori) fixed.**



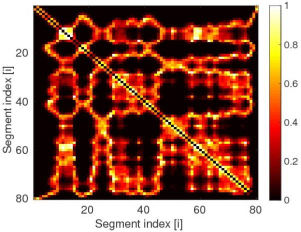
Ori free for *E.coli*

**12 independent Initial Conditions.**

# Positional Corr of CC: Confinement + Crowders



No crowder
$R_c = 5a = 0.55R_g$.



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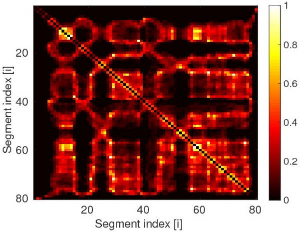
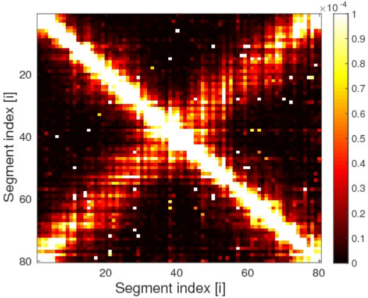


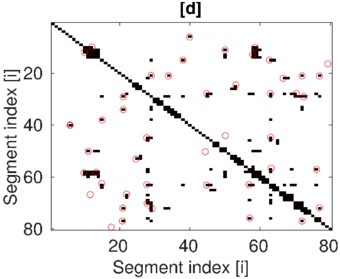
Crowder: Weak Attraction
LJ $\epsilon = 0.3k_BT$.

**Crowder:**
**The presence of other organelles within cell compactifies DNA: modelled by weak effective attraction between monomers**.

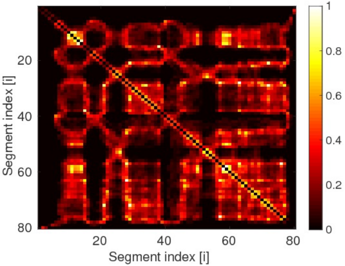
# CC : Comparison with experiments: confinement+crowders



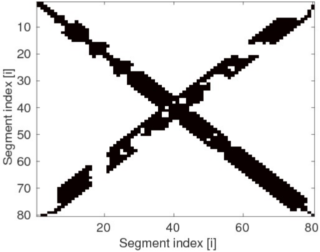
(**Experimental coarse-grained**)



OFF-diagonal $p(i,j) > 0.5$: BLACK



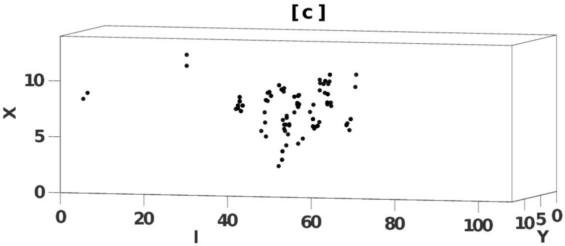
SIMULATIONS:



Diagonals $p(i,j) > 0.05$: BLACK

# CONCLUSIONS:

Self avoiding loops emanating from cluster of cross-links: CLs are clustered around center.



- **33,38 Cross-links + Confinement + Crowder organize DNA (micron scale) for 2 bacteria: C. crescentus and E. coli.**
- **We give 3-d prediction of local position of segments within Cell.**
- **EPL (2018), JPCM (2018), arxiv: 1808.09400, 1808.09396.**

**THANK YOU FOR YOUR ATTENTION**