Knots and Links: From Form to Function

Numerical Knots: Models and Simulations Workshop
Centro di Ricerca Matematica Ennio De Giorgi
Scuola Normale Superiore, Pisa, Italy
June 8 & 9, 2011

PROGRAM

June 8:	8:45 – 9:00	Welcome and Introduction	
	9:00-10:00	Plenary Lecture 1	Doros Theodorou
	10:00-10:15	Pause	
	10:15-11:15	Plenary Lecture 2	Mariel Vazquez
	11:15-11:30	Pause	
	11:30-12:30	Plenary Lecture 3	Eric Rawdon
	12:30-14:30	Lunch	
	14:30-15:30	Plenary Lecture 4	Cristian Micheletti
	15:30-15:45	Pause	
	15:45-16:45	Plenary Lecture 5	Peter Virnau
	16:45-17:00	Pause	
	17:00-18:00	Plenary Lecture 6	Rob Scharein
	18:00-18:15	Pause	
	18:15-18:45	Short Lecture 1	Christos Tzoumanekas
	18:45-19:15	Short Lecture 2	Luca Tubiana
	19:30	Dinner	

June 9:	9:00-10:00	Plenary Lecture 7	Enzo Orlandini
	10:00-10:15	Pause	
	10:15-11:15	Plenary Lecture 8	Chris Soteros
	11:15-11:30	Pause	
	11:30-12:30	Plenary Lecture 9	Andrew Rechnitzer
	12:30-14:30	Lunch	
	14:30-15:00	Short Lecture 3	Eleni Panagiotou
	15:00-15:30	Short Lecture 4	Guillame Witz
	15:30-15:45	Pause	
	15:45-16:45	Plenary Lecture 10	Ken Millett
	16:45-17:00	Pause	
	17:00-19:30	Poster Session/Discussion	
	19:30	Dinner	

Lecture Titles and Abstracts

Cristian Micheletti, International school for Advanced Studies (SISSA), Trieste, Italy
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DNA knotting inside viral capsids: a computational approach

The packing of DNA inside bacteriophages arguably yields the simplest example of genome organisation in living organisms [1, 2]. An indirect indication of how DNA is packaged is provided by the detected spectrum of knots formed by DNA that is circularised inside the P4 viral capsid [3, 4]. The experimental results on the knot spectrum of the P4 DNA are here compared to results of coarse-grained simulation of DNA knotting in confined volumes. We start by considering a standard coarse-grained model for DNA which is known to be capable of reproducing the salient physical aspects of free, unconstrained DNA [5]. Specifically the model accounts for DNA bending rigidity and excluded volume interactions. By subjecting the model DNA molecules to spatial confinement it is found that confinement favours chiral knots over achiral ones, in agreement with P4 experiments. However, no significant bias of torus over twist knots is found, contrary to what found in P4 experiments [6, 7]. A good agreement with experiment is found, instead, upon introducing an additional interaction potential that accounts for tendency of contacting DNA portions to order as in cholesteric liquid crystals. Accounting for this local potential allows us to reproduce the main experimental data on DNA organization in phages, including the cryo-EM observations and detailed features of the spectrum of DNA knots formed inside viral capsids. The DNA knots we observe are strongly delocalized and, intriguingly, this is shown not to interfere with genome ejection out of the phage [8].

References

[1] Earnshaw WC, Harrison SC (1977) DNA arrangement in isometric phage heads. Nature 268:598-602.
[2] Gelbart WM, Knobler CM (2009) Virology. pressurized viruses. Science 323:1682-1683.
[3] Arsuaga J, Vazquez M, Trigueros S, Sumners D, Roca J (2002) Proc Natl Acad Sci U S A 99:5373-5377.
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[5] Rybenkov VV, Cozzarelli NR, Vologodskii AV (1993) Proc Natl Acad Sci U S A 90:5307-5311.
[6] Micheletti C, Marenduzzo D, Orlandini E, Sumners DW (2006) J Chem Phys 124:64903-64903.
[7] Micheletti C, Marenduzzo D, Orlandini E, Sumners DW (2008) Biophys J 95:3591-3599.
[8] Marenduzzo D, Orlandini E, Stasiak A, Sumners DW, Tubiana L, Micheletti C (2009) Proc Natl Acad Sci U S A 106:22269-22274.

Kenneth C. Millett, Department of Mathematics, University of California, Santa Barbara, CA, USA

The Random Generation of Equilateral Polygonal Knots

Two strategies of generating random equilateral closed polygons employ polygonal folds and crankshaft rotations as their basic operation. The two methods will be described and their implementations compared via several applications to the study of the average properties of knot space. This is joint work with Sotero Alvarado and Jorge Alberto Calvo.

Enzo Orlandini, INFN e Dipartimento di Fisica, Università di Padova

Polymers with spatial and geometrical constraints: theoretical and computational results

The understanding of the equilibrium properties of polymers subject to geometrical constraints is an area of primary interest in physics, mathematics, chemistry, mathematics and life sciences. The interest in the area has been recently boosted by a number of major experimental advancements based on single-molecule manipulation and advanced imaging techniques. These experiments provide a rapidly-growing amount of detailed characterizations of the interplay between the polymer entanglement and the geometrical confinement which call for a thorough understanding and interpretation by means of suitable mesoscopic models. For linear polymers some progress have been made in terms both of efficient stochastic simulations and of simple scaling arguments based on the competition between the polymer average size and the typical size of the confining region. The situation is less clear when rings are under confinement. In this case the presence of topological entanglements (knots or links) introduces a further length scale (topological) into the problem which, by competing with the other two lengths scales, may affect both the topological properties (when free to vary) of the rings and their overall shape (at fixed topology).

In this talk we review some available theoretical and computational progress that have been made in the last few years on this subject. In particular we introduce and describe some stochastic methods for sampling coarse grained models of polymers under confinement and discuss their efficiency as the size of the confining region decreases. Finally, by focussing on the problem of linear and circular chains confined into slits we present recent results concerning i) the effect of confinement on the conformational properties of polymers with fixed topology and ii) the effect of spatial confinement on polymers' equilibrium topology.

Eleni Panagiotou, Department of Mathematics, National Technical University of Athens, 9 Heroon Polytechniou Street, Zografou Campus, 157 80 Athens, Greece

A study of the linking number in systems with periodic boundary conditions

In this talk we give a new definition for the linking number between two oriented closed or open chains in a system with three-dimensional periodic boundary conditions (PBC), and of the self-linking number and the writhe of one oriented

closed or open chain in a system with three PBC. Furthermore, we show how this definition of the linking number, for two oriented closed chains in a system with PBC, coincides with the Gauss linking number of two oriented closed chains in 3-space, and also with the Gauss linking number of two oriented closed chains in a 3-manifold. This definition is suitable for studying entanglement in a collection of closed, or open polymer chains, as they are given by a computer generated atomistic polymer sample. Using this new measure of linking for chains in systems with three PBC, we study numerically the effect of CReTA (Contour Reduction Topological Analysis) algorithm on the entanglement of polyethylene chains. Our results show that the new linking measure is consistent for the original and reduced systems. It can be used to characterize entanglement under periodic boundary conditions.

Eric Rawdon, Department of Mathematics, University of St. Thomas , St. Paul, MN, USA

Knotted Arcs in Polymer Models

Some proteins have been classified recently as being knotted. However, proteins have free ends and knotting, traditionally, has only been defined formally for closed curves. How should we define the existence of knotting within open chains? Once we settle on a definition, we can search for smallest knotted arcs within knotted open and closed chains. We discuss generating polymer models and show recent results for classifying the knotting within models and within proteins. This is joint work with Ken Millett, Andrzej Stasiak, and Joanna Sulkowska.

Andrew Rechnitzer, Department of Mathematics, The University of British Columbia, Vancouver, BC, Canada

Counting polygons and knots

Self-avoiding polygons are simple closed curves embedded in a regular lattice. They belong to a family of objects, known collectively as lattice animals, that lie at the heart of lattice models of polymers, magnets and other phenomena. This large family of discrete structures has been a source of combinatorial problems for over 50 years and many basic questions remain stubbornly unsolved. For example, the simple enumerative question - "How many self-avoiding polygons are there of length n?" is currently best answered by an algorithm that requires exponential time and memory.

The question of counting polygons on the cubic lattice is enriched by topology - self-avoiding polygons have well defined knot types. The exact computation of the number of polygons of length n and fixed knot type K is extremely difficult - indeed the current best algorithms can barely touch the first knotted polygons. In this talk I will discuss a different approach to the problem. Instead of of exact methods, we have used an approximate enumeration method - which we call the GAS algorithm. This is a generalisation of the famous Rosenbluth method for sampling self-avoiding walks.

Using this algorithm we have estimated the number of polygons of different lengths

and knot types on three different cubic lattices. These give direct evidence that the asymptotic growth of the number of polygons of a fixed knot type K is simply related to the growth of the number of unknotted polygons and the number of prime components in K. We have also studied the relative frequencies of different knots - for example, the ratio of the number of trefoils to the number of figure-eights. We see strong evidence that these ratios are universal suggesting that a very long closed curve is about 27 times more likely to be a trefoil than a figure-eight.

Rob Scharein, Hypnagogic Software & San Francisco State University, San Francisco, CA, USA

Computational Knot Theory with KnotPlot

When experimenting with knots on a computer, it is useful to have powerful tools for the creation of initial conformations, for performing simulations on those conformations and also to compute topological and geometric properties of any resulting products.

KnotPlot is one such tool that has been invaluable in the speaker's own research into minimal stick conformations of knots in R^3 and on the lattice. After a brief review of these projects and several others involving the simplification of very complex knots, we will explore features within KnotPlot, some new and some old, that allow a wide range of interesting experiments to be performed.

Chris Soteros, Department of Mathematics and Statistics, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

Knotting probabilities after a local strand passage in unknotted self-avoiding polygons

M. Szafron and I have developed a self-avoiding polygon model of local strand passage which allows for the investigation of knot distributions after a unidirectional crossing-sign change at the strand-passage-site. The model is used to explore possible mechanisms for the experimentally observed unknotting efficiency and chirality discrimination of type 2 topoisomerase action on DNA. A composite Markov Chain Monte Carlo (CMC) BFACF-based algorithm, called the CMC θ-BFACF algorithm, is used to investigate the model. In this talk, I will define the model, present theoretical results related to it, and then describe the CMC θ-BFACF in detail. I will outline the ergodicityproof and statistical methods for analyzing the data generated from the algorithm. Finally, I will present results about the knotting probabilities after a local strand passage in unknotted self-avoiding polygons.

Doros N. Theodorou, School of Chemical Engineering, National Technical University of Athens, 9 Heroon Polytechniou Street, Zografou Campus, 157 80 Athens, Greece, doros@central.ntua.gr

Searching for entanglements in atomistic simulations of polymer melts

The recent development of connectivity-altering Monte Carlo algorithms has enabled efficient sampling of the complex configuration spaces of dense, long-chain polymers and equilibration of atomistic models of such polymers at all length scales. We will discuss the geometric and statistical mechanical underpinnings of these algorithms, present predictions obtained from them concerning the structure, conformation, and thermodynamic properties of specific polymer melts, and compare these predictions to experimental measurements. We will also discuss the Contour Reduction Topological Analysis (CReTA) algorithm, whereby well-equilibrated atomistic configurations of linear chains are reduced to networks of entangled "primitive paths". The statistical segment length of these primitive paths serves as an excellent estimate of the "tube diameter" invoked in theories of polymer melt deformation and flow.

Luca Tubiana, International school for Advanced Studies (SISSA), Trieste, Italy

Probing the entanglement and locating knots in ring polymers: a comparative study of different arc closure schemes.

The interplay between the topological and geometrical properties of a polymer ring can be clarified by establishing the entanglement trapped in any portion (arc) of the ring. The task requires closing the open arcs into a ring, and the resulting topological state may depend on the specific closure scheme that is followed. To understand the impact of this
ambiguity in contexts of practical interest, such as knot localization in a ring with non trivial topology, we apply various closure schemes to model ring polymers. The comparison suggests that a novel method, called the minimally-interfering closure, can be
profitably used to characterize the arc entanglement in a robust and computationally-efficient way. This closure method is applied to the knot localization problem which is tackled using two different localization schemes based on top-down or bottom-up searches.

Christos Tzoumanekas, Department of Materials Science and Engineering, School of Chemical Engineering, National Technical University of Athens, Zografou Campus, 15780 Athens, Greece and Dutch Polymer Institute (DPI), P.O. Box 902, 5600 AX Eindhoven, The Netherlands, tzoumanekas@gmail.com

From rods to random walks: Onset of entanglements in linear polymer melts. Topological and dynamical aspects.

It has long been known that the variation of density and stiffness between different species signifies changes in the degree of entanglement of long-chain flexible polymer melts. An overlooked point is that, as chain length *N* increases, the contour length density (or mass density), and the stiffness of the system (or characteristic ratio), increase, until they reach chain length-independent values (large *N* asymptotic regime). Here we examine how the variation of these quantities, as chain length increases, is related with the onset of entanglements, and the associated changes in the underlying system topology.

Our analysis is based on the reduction of Dissipative Particle Dynamics trajectories of a coarse-grained polymer melt to Primitive Paths (PPs). The latter are generated by using the CReTA algorithm, which constructs PPs by reducing chain conformations to the corresponding shortest paths.
We will show that, as N increases, the density and stiffness exhibit an N-dependence which leads to larger chain overlap in the short, than in the long chain regime. For large N, chain overlap falls gradually to the scaling law expected of long-chain systems.
At the level of PPs, the increasing overlap leads to a crossover in the system topology which can be described as a gradual transformation of PP conformations from thin rods (short chains), to random walks (long chains), A simple scaling model predicts that this transformation leads to a Rouse to reptation transition in dynamics and rheology. The entanglement molecular weight (MW), M_e is interpreted as the crossover length of this transition. The predicted critical to entanglement MW ratio, M_c / M_e is one, which, though small, is compatible with packing length independence and the suppression of contour length fluctuations within the model. The comparison between a dynamical and a static topological analysis reveals a slowing down of Rouse modes, which is maximum at the length scale where the underlying system of PPs appears as a network of topological constraints.

References : *Macromolecules* 42, 7474, (2009) ; *ibid.* 42, 7485, (2009)

Mariel Vazquez, Department of Mathematics, San Francisco State University, California, USA

Random knots and confinement considerations

DNA presents high levels of condensation in all organisms. We are interested in the problem of DNA packing inside bacteriophage capsids. Bacteriophages are viruses that infect bacteria. DNA extracted from bacteriophage P4 capsids is highly knotted. Here use the packing of P4 DNA to motivate a couple of recent lines of work in our group. First, it is interesting to ask what is the minimal length of DNA needed to tie a particular knot type. Following on the steps of Y. Diao and of E.J. Janse van Rensburg, we have characterized both analytically and numerically the minimum length (also called minimum step number) needed to form a particular knot in the simple cubic lattice. Second, suppose that we are dealing with a set of random polygons with the same length and knot type, which could be the model of some circular DNA with the same topological property. In general, a simple way of detecting chirality of this knot type is to compute the mean writhe of the polygons; if the mean writhe is non-zero then the knot is chiral. Furthermore, we conjecture that the sign of the mean writhe is a topological invariant of chiral knots. We provide numerical evidence to support these claims, and we propose a new nomenclature of knots based on the sign of their expected writhes. This nomenclature can be of particular interest to applied scientists. This is joint work with Javier Arsuaga, Yuanan Diao, Kai Ishihara,

Juliet Portillo, Rob Scharein, De Witt Sumners and Koya Shimokawa

Peter Virnau, Institute of Physics, Johannes Gutenberg-Universitat, Mainz, Germany

On entanglements in polymer chains, melts, brushes and proteins

The determination of knots provides a measure for entanglement in single polymer chains akin to concepts like the primitive path in melts. In the first part of my talk I will investigate coarse-grained polymer models with Monte Carlo simulations and discuss the influence of solvent quality, confinement, stiffness and sequence on entanglements as well as implications for DNA and proteins. I will also give a short overview of knots in proteins with a focus on structures discovered recently. In the second part of my talk, I will present recent molecular dynamics simulations of unknotted (closed) polymer loop melts and loop brushes using a fast implementation on graphics processing units (GPUs). Melts of polymer loops have been discussed recently as a simplistic model for the formation of chromosome territories in the interphase. Particular attention will be paid to scaling relations. In this context I will also present measurements relating the computing performance of a single consumer graphic card to conventional state of the art supercomputers.

Guillaume Witz, EPFL, Lausanne, Switzerland

Structure and dynamics of supercoiled knots and catenanes

Circular DNA molecules *in vivo* form catenanes and knots during processes like replication or recombination. In addition, DNA molecules are often subjected to a torsional tension, which results in their supercoiling. The interplay between catenation, knotting and supercoiling leads to unexpected conformational changes of the DNA molecules, with interesting physical and biological consequences. In particular, the behavior of DNA molecules in the widely used technique of gel electrophoresis depends on these structural changes, which have therefore to be thoroughly understood. Using numerical simulation techniques where DNA is modeled as a semi-flexible ribbon, and where hydrodynamic interactions can be taken into account, we analyzed both the conformation and the sedimentation behavior of supercoiled molecules with complex topologies. The results that will be presented especially highlight the importance of the chirality of knots and catenanes in the structural changes induced by DNA supercoiling. For example, strongly linked right-handed toroidal DNA catenanes undergo a specific folding that can be reversed by the introduction of negative supercoiling in each chain, and the shape of negatively supercoiled DNA trefoil knots depends on their chirality. Comparison with experimental data, and biological consequences of the observe phenomena will also be presented.