Banff International Research Station
for Mathematical Innovation and Discovery

Mathematics of Knotting and Linking in Polymer Physics and Molecular Biology
May 21 - 25, 2007

MEALS

*Breakfast (Buffet): 7:00 – 9:00 am, Donald Cameron Hall, Monday – Friday
*****Lunch (Buffet): 11:30 am – 1:30 pm, Donald Cameron Hall, Monday – Friday
*****Dinner (Buffet): 5:30 – 7:30 pm, Donald Cameron Hall, Sunday – Thursday
Coffee Breaks: As per daily schedule, 2nd floor lounge, Corbett Hall
***Please remember to scan your meal card at the host/hostess station in the dining room for each meal.**

MEETING ROOMS

All lectures will be held in Max Bell 159 (Max Bell Building accessible by bridge on 2nd floor of Corbett Hall). Hours: 6 am – 12 midnight. LCD projector, overhead projectors and blackboards are available for presentations. *Please note that the meeting space designated for BIRS is the lower level of Max Bell, Rooms 155-159. Please respect that all other space has been contracted to other Banff Centre guests, including any Food and Beverage in those areas.*

SCHEDULE

Sunday May 20, 2007

16:00	Check-in begins (Front Desk – Professional Development Centre - open 24 hours)
17:30-19:30	Buffet Dinner, Donald Cameron Hall
20:00	Informal gathering in 2nd floor lounge, Corbett Hall Beverages and small assortment of snacks available on a cash honour-system.

Monday May 21, 2007

7:00-8:45	Breakfast		
8:45-9:00	Introduction and Welcome to BIRS by BIRS Station Manager, Max Bell 159		
9:00 - 10:00	Lecture 1	Zechiedrich	*DNA entanglement and resolution; A matter of life, death, and evolution*
10:00 - 10:30	Coffee		
10:30 - 11:00	Lecture 2	Vologodskii	*Statistical-mechanical analysis of enzymatic topological transformations in DNA molecules*
11:00 - 11:30	Lecture 3	Chan	*The statistical mechanics of how recognition of local DNA juxtaposition geometry may underlie the unknotting and decatenating actions of type-II topoisomerases*
11:30 - 12:45	Lunch		
12:45 - 13:30	Tour		
13:30 - 14:00	Group Photo		
14:00 - 14:30	Lecture 4	Vazquez	*Modelling DNA topology simplification*
14:30 - 15:00	Lecture 5	Soteros	*Asymptotics of Knotting After a Local Strand Passage*
15:00 - 15:30	Lecture 6	Mann	*Human Topoisomerase IIalpha Resolves DNA Twist Knots in a Single Ste*
15:30 - 16:00	Coffee		
16:00 - 16:30	Lecture 7	Stasiak	*Model of selective simplification of DNA topology by DNA topoisomerases*
16:30 - 17:30	Discussion		
17:30 - 19:30	Dinner		

Tuesday May 22, 2007

7:00-9:00	Breakfast		
9:00 - 10:00	Lecture 8	Orlandini	*Topological effects on the dynamics of knotted polymers*
10:00 - 10:30	Coffee		
10:30 - 11:00	Lecture 9	Tesi	*Knot Probability and Stretching*
11:00 - 11:30	Lecture 10	van Rensburg	*Squeezing knotted polygons in a slab*
11:30 - 13:30	Lunch		
13:30 - 14:30	Lecture 11	Sumners	*DNA knots reveal chiral packing of DNA in phage capsids*
14:30 - 15:00	Lecture 12	Arsuaga	*Topological considerations of the interphase nucleus*
15:00 - 15:30	Lecture 13	Darcy	*Modeling protein-DNA complexes in 3D with TopoICE: Topological Interactive Construction Engine*
15:30 - 16:00	Coffee		
16:00 - 16:30	Lecture 14	Buck	*A model of DNA knotting and linking: biological argument*
16:30 - 17:00	Lecture 15	Flapan	*A model of DNA knotting and linking: topological argument*
17:00 - 17:30	Discussion		
17:30 - 19:30	**BANQUET**		

Wednesday May 23, 2007

7:00-9:00	Breakfast		
9:00 - 10:00	Lecture 16	Grosberg	*Metastable Tight Knots in a Worm-like Polymer*
10:00 - 10:30	Coffee		
10:30 - 11:00	Lecture 17	Duplantier	*Closed Random Walks*
11:00 - 11:30	Lecture 18	Deguchi	*Dynamics and statistical mechanics of knotted ring polymers in solution: a simulation approach towards experimental confirmation of topological effects*
11:30 - 12:00	Lecture 19	Millett	*How many knots are enough?*
12:00 - 13:30	Lunch		
13:30 - 17:30	Free Afternoon		
17:30 - 19:30	Dinner		

Thursday May 24, 2007

7:00-9:00	Breakfast		
9:00 - 10:00	Lecture 20	Maddocks	*Ideal Knots in the 3-Sphere*
10:00 - 10:30	Coffee		
10:30 - 11:00	Lecture 21	Gerlach	*Optimal Tube Packing in the 2-sphere*
11:00 - 11:30	Lecture 22	Kusner	*Lengths of knotted bands and raceways*
11:30 - 13:00	Lunch		
13:30 - 14:00	Lecture 23	Stella	*Ranking knots of random, globular polymer rings*
14:00 - 14:30	Lecture 24	Rechnitzer	*Mean unknotting times of random knots and embedding*
14:30 - 15:00	Lecture 25	Simon	*Measuring tangling in large filament systems*
15:00 - 15:30	Lecture 26	Cantarella	*Modelling Very Large Macromolecules as Vector Fields*
15:30 - 16:00	Coffee		
16:00 - 16:30	Lecture 27	Ernst	*Knotting on cubic lattice*
16:30 - 17:00	Lecture 28	Whittington	*Random knotting: what we know and what we think we know*
17:00 - 17:30	Discussion		
17:30 - 19:30	Dinner		

Friday May 25, 2007

7:00-9:00	Breakfast		
9:00 - 9:30	Lecture 29	Dietler	*Fractal Dimension and Localization of DNA Knots*
9:30 - 10:00	Lecture 30	Micheletti	*Knotting of random ring polymers in confined spaces*
10:00 - 10:30	Coffee		
10:30 - 11:00	Lecture 31	Diao	*Sampling Large Random Knots in a Confined Space*
11:00 - 11:30	Lecture 32	Rawdon	*Equilibrium Lengths of Random Equilateral Polygons*
11:30 - 13:00	Lunch	**Checkout of guest rooms promptly by 12 noon is required**	
13:00 - 15:00	Open Discussion**		
15:00	Depart		

Checkout by 12 noon!

** 5-day workshops are welcome to use the BIRS facilities (2nd Floor Lounge, Max Bell Meeting Rooms, Reading Room) until 3 pm on Friday, although *participants are still required to checkout of the guest rooms by 12 noon*. **

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ABSTRACTS

Speaker: Javier **Arsuaga** (San Francisco State University)
Title: *Topological considerations of the interphase nucleus*
Abstract: During the early phase of the cell cycle (G0/G1) chromosomes are confined to spherical regions within the nucleus called chromosome territories. The position of these territories is important in a number of biological processes (e.g. transcription, replication and DNA repair) and has important implications in human genetic diseases, in cancer and in the formation of chromosome aberrations after exposure to DNA damaging agents. It has been recently proposed a model for the interface region between territories in which chromosomes overlap and intermingle (Branco and Pombo, 2006). This new model naturally raises the question of whether chromosomes are linked or not. Motivated by this problem we investigated the linking of curves in confined volumes. In this talk I will present our recent results using the uniform random polygon model. First we analytically show that the linking probability between a fixed closed curve and a random polygon of length n increases as 1- O((1/n)^1/2). Next we show numerically that the linking probability between two polygons of lengths n and m increase as 1- O((1/nm)^1/2). We also extend these results to the case when two polygons have a predetermined overlapping volume (as is the case in experimental observations). We conclude by discussing potential extensions to other polymer models and biological implications.

Speaker: Dorothy **Buck** (Imperial College London)
Title: *A model of DNA knotting and linking: biological argument*
Abstract: We present a topological model that predicts which knots and links are the products of site-specific recombination. We do this by describing the topology of how DNA knots and links are formed as a result of a single recombination event, or multiple rounds of (processive) recombination events, starting with substrate(s) consisting of an unknot, an unlink, or a (2, n)-torus knot or link. Our model relies on only three assumptions and we give biological evidence for each of these assumptions. This talk will present the biological background, evidence, and applications of our model. Note this talk will be integrated with the talk of Erica Flapan.

Speaker: Jason **Cantarella** (University of Georgia)
Title: *Modelling very large macromolecules as vector fields*
Abstract: This talk is meant as an (mostly expository) invitation to the community interested in modeling large molecules to consider an alternate mathematical framework for their work: modeling large macromolecules as divergence-free vector fields instead of as curves, polygons, chains, or tubes. From this point of view, the actual topological knot type of a very large and complicated curve will be seen as less important than its average entanglement complexity.

The talk will introduce this framework, review some older results about the helicity of vector fields (which measures a kind of average linking number of integral curves), outline some very speculative applications to macromolecules, and introduce some work in progress reformulating the helicity of vector fields from a more modern perspective. Our reformulation of helicity opens the possibility of constructing a family of ``generalized helicity'' integrals analogous to finite-type invariants for knots.

Speaker: Hue Sun **Chan** (University of Toronto)
Title: The Statistical Mechanics of How Recognition of Local DNA Juxtaposition Geometry May

Underlie the Unknotting and Decatenating Actions of Type-II Topoisomerases
Abstract: Topoisomerases may unknot and decatenate by recognizing specific DNA juxtapositions [Buck & Zechiedrich, J Mol Biol 340, 933-939 (2004)]. The statistical mechanical viability of this hypothesis was investigated by considering lattice models of single-loop conformations and two-loop configurations of ring polymers. Using exact enumerations and Monte Carlo sampling, we determined the statistical relationship, between the local geometry of a juxtaposition of two chain segments on one hand, and whether a single loop was knotted or whether two loops were linked globally on the other; and ascertained how the knot/unknot topology and global linking were altered by a topoisomerase-like segment passage at the juxtaposition. We found that segment passages at a "free" juxtaposition tend to increase knot probability but segment passages at a "hooked" juxtaposition cause more transitions from knot to unknot than vice versa, resulting in a steady-state knot probability far lower than that at topological equilibrium. Similarly, our results indicated that selective segment passage at hooked juxtapositions could lower catenane populations significantly. A general
exhaustive analysis of ~6,000 different juxtaposition geometries showed that the ability of a segment passage to unknot and decatenate correlates strongly with a juxtaposition's "hookedness." Most remarkably, and consistent with experiments on type-2 topoisomerases from different organisms by Cozzarelli and coworkers [Rybenkov et al., Science 227, 690-693 (1997)], the unknotting potential of a juxtaposition geometry in our polymer model correlates almost perfectly with its corresponding decatenation potential, with a scaling exponent quite similar to that observed in experiments. These quantitative findings suggest that it is possible for type-II topoisomerases to disentangle by acting selectively on juxtapositions with hook-like geometries. If time permits, I will also discuss additional results from the ongoing extensions of our general approach to rationalize other experimental aspects of type-II topoisomerase actions.

Speaker: Isabel **Darcy** (University of Iowa)
Title: *Modeling protein-DNA complexes in 3D with TopoICE: Topological Interactive Construction Engine*
Abstract: Protein-DNA complexes have been modeled using tangles. A tangle consists of arcs properly embedded in a 3-dimensional ball. The protein is modeled by the 3D ball while the segments of DNA bound by the protein can be thought of as arcs embedded within the protein ball. This is a very simple model of protein-DNA binding, but from this simple model, much information can be gained. The main idea is that when modeling protein-DNA reactions, one would like to know how to draw the DNA. For example, are there any crossings trapped by the protein complex? How do the DNA strands exit the complex? Is there significant bending? Tangle analysis cannot determine the exact geometry of the protein-bound DNA, but it can determine the overall entanglement of this DNA, after which other techniques may be used to more precisely determine the geometry. KnotPlot, developed by Rob Scharein, is an interactive 3D program for visualizing and manipulating knots. TopoICE-X is a subroutine within KnotPlot for solving tangle equations modeling topoisomerase reactions.

Speaker: Tetsuo **Deguchi** (Ochanomizu University)
Title: *Dynamics and statistical mechanics of knotted ring polymers in solution: a simulation approach towards experimental confirmation of topological effects*
Abstract: We discuss how topological effects may give nontrivial results on the macroscopic behavior of ring polymers in solution and how we can confirm them experimentally. We discuss numerical evaluation of some characteristic physical quantities of the solution that can be measured in polymer experiments. The present study is strongly motivated by recent experimental developments for synthesizing ring polymers with large molecular weights. We present some numerical results on dynamical and statistical properties of a dilute solution of ring polymers where topological constraints play a central role. First, we discuss dynamical quantities such as the diffusion constants of ring polymers in solution and the viscosity of the ring-polymer solution, and show how they are different from those of the corresponding linear polymers with the same molecular weights. Secondly, the osmotic pressure of the ring-polymer solution reflects the topological interaction among ring

polymers, and it is numerically evaluated in terms of the random linking probability. Thirdly, the mean square radius of gyration of ring polymers under a topological constraint, which is one of the most fundamental quantities in the physics of knotted ring polymers, can be measured in the scattering experiment. The single-chain static structure factor, i.e. the scattering function, can be obtained experimentally for ring polymers with fixed topology, from which we derive the mean square radius of gyration. It is therefore important to evaluate numerically the scattering function of a knotted ring polymer in solution, and we discuss some theoretical and simulational results on the scattering functions.

Speaker: Giovanni **Dietler** (Ecole Polytechnique Federale de Lausannne)
Title: Fractal dimension and localization of DNA knots
Abstract: The properties of knotted DNA in respect to the critical exponents and the localization of the knot crossings will be reported: I will show that probably two universality classes exist in this case and that localization of the knot crossings could explain the activity of the topoisomerases. Then gel electrophoresis of DNA knots will be discussed and simulation as well as experiments will be presented where the knot complexity and its topology play an essential role. Some hydrodynamics experiments with knots will be presented at the end of the lecture.

Speaker: Yunan **Diao** (University of North Carolina)
Title: *Sampling Large Random Knots in a Confined Space*
Abstract: We propose the 2-dimensional uniform random polygons as an alternative method of sampling large random knot diagrams. In fact, the 2-dimensional uniform random polygons allow us to sample knot diagrams with large crossing numbers that are diagrammatically prime since we can rigorously prove that the probability that a randomly selected 2-D uniform random polygon of n vertices is almost diagrammatically prime (in the sense that the diagram becomes a reduced prime diagram after a few third Reidemeister moves) goes to one as n goes to infinity, and that the average number of crossings in such a diagram is at the order of $O(n^2)$. This strongly suggests that the 2-Dimensional uniform random polygons are good candidates if one is interested in sampling large (prime) knots. Numerical studies on the 3-D uniform random polygons show that these polygons for complicated knots even when they have relatively small number of vertices.

Speaker: Bertrand **Duplantier** (Saclay)
Title: Random Linking of Curves and Manifolds
Abstract: We propose a formalism for evaluating random linking integrals of closed curves in R^3 or, more generally, manifolds in R^n, all in relative motions. It is based on the existence of universal geometric characteristic functions for each closed curve or manifold separately. It allows further averaging over the possible random shapes of those curves and manifolds.

Speaker: Claus **Ernst** (Western Kentucky University)
Title: Knotting on cubic lattice
Abstract: Summary of what is currently known about the topological aspects of lattice knots such as their length and curvature. The length as braids is also considered.

Speaker: Erica **Flapan** (Pomona College)
Title: *A model of DNA knotting and linking: topological argument*
Abstract: We present a topological model that predicts which knots and links can be the products of site-specific recombination. We do this by describing the topology of how DNA knots and links are formed as a result of a single recombination event, or multiple rounds of (processive) recombination events, starting with substrate(s) consisting of an unknot, an unlink, or a (2, n)-torus knot or link. Our model relies on only three assumptions and we give biological evidence for each of these assumptions. This talk will present the topological argument for our model. Note this talk will be integrated with the talk of Dorothy Buck.

Speaker: Henryk **Gerlach** (Ecole Polytechnique Federale de Lausannne)
Title: Optimal Tube Packing in the 2-sphere
Abstract: Some results concerning optimal packing of tubes constrained to lie on the 2-sphere. (provided by KCM)

Speaker: Alexander **Grosberg** (University of Minnesota)
Title: Metastable Tight Knots in a Worm-like Polymer
Abstract: Based on an estimate of the knot entropy of a worm-like chain we predict that the interplay of bending energy and confinement entropy will result in a compact metastable configuration of the knot that will diffuse, without spreading, along the contour of the semi-flexible polymer until it reaches one of the chain ends. Our estimate of the size of the knot as a function of its topological invariant (ideal aspect ratio) agrees with recent experimental results of knotted dsDNA. Further experimental tests of our ideas are proposed.

Speaker: Rob **Kusner** (University of Massachusetts)
Title: *Lengths of knotted bands and raceways*
Abstract: We consider geometric problems for embedded bands in space. Just as we can minimize the ropelength for knotted or linked space curves, we can also minimize the analogous "bandlength" for smoothly framed curves, either within a framed isotopy class, or with a pointwise constraint on the framing (which we view as a normal vector field along the corresponding bands). As a limiting case where the framing for the bands is constant, we get knotted or linked "raceways" in the plane, a flattened analogue of knotted or linked "ropes" in space. We show that the bandlength of raceways grows at least as fast as the square root of crossing number (recall that for ropes we had instead the three-fourths power) and that this power is sharp. We also comment on the shapes of length-minimizing raceways, and speculate on bands or raceways as models for folded or packed proteins.

Speaker: John **Maddocks** (Ecole Polytechnique Federale de Lausannne)
Title: *Ideal Knots in the 3-sphere*
Abstract: The radius of the 3-sphere introduces a third length scale into the ideal shape problem in addition to arc length and thickness that breaks the dilation symmetry of Euclidean 3-space. This implies that, in the 3-sphere, there are three distinct natural notions of ideality. The same breaking of symmetry arises in optimal packings in confined geometries. (provided by KCM)

Speaker: Jennifer **Mann** (Florida State University)
Title: *Human Topoisomerase IIα Resolves DNA Twist Knots in a Single Step*
Abstract: Cellular DNA knotting is driven by DNA compaction, topoisomerization, replication, supercoiling-promoted strand collision, and DNA self-interactions resulting from transposition, site-specific recombination, and transcription. Type II topoisomerases are ubiquitous, essential enzymes that interconvert DNA topoisomers to resolve knots. These enzymes pass one DNA helix through another by creating an enzyme-bridged transient break. We investigate how type II topoisomerases accomplish their unknotting feat.

Will a type II topoisomerase resolve a DNA twist knot in one cycle of action? Each crossing reversal performed by a type II topoisomerase requires energy. Within the cell, DNA knots might be pulled tight by forces such as those that accompany transcription, replication, and segregation, thus increasing the likelihood of DNA damage. Our results show DNA knots can be lethal and promote mutations. Therefore, it would be advantageous for type II topoisomerases to resolve DNA knots in the most efficient manner. My data show that purified five- and seven-noded twist knots are converted to the unknot by human topoisomerase II□ with no appearance of either trefoils or five-noded twist knots which are intermediates if the enzyme acted on one of the interwound nodes.

Speaker: Cristian **Micheletti** (International School for Advanced Studies)
Title: *Knotting of random ring polymers in confined spaces*

Abstract: Stochastic simulations are used to characterize the knotting distributions of random ring polymers confined in spheres of various radii. The approach is based on the use of multiple Markov chains and reweighting techniques, combined with effective strategies for simplifying the geometrical complexity of ring conformations without altering their knot type. By these means we extend previous studies and characterize in detail how the probability to form a given prime or composite knot behaves in terms of the number of ring segments N and confining radius R. For $50 \leq N \leq 450$ we show that the probability of forming a composite knot rises significantly with the confinement, while the occurrence probability of prime knots are, in general, nonmonotonic functions of 1/R. The dependence of other geometrical indicators, such as writhe and chirality, in terms of R and N is also characterized. It is found that the writhe distribution broadens as the confining sphere narrows

Speaker: Kenneth **Millett** (University of California, Santa Barbara)
Title: *How many knots are enough?*
Abstract: This question addresses the problem of estimating the number of distinct topological knot types and their proportion in the space of (equilateral) polygonal knots with a fixed number of edges. For very small numbers of edges, one knows the number of knot types and can estimate their proportion but, for larger numbers of edges, only rough estimates are available. Estimates derive from Monte Carlo explorations of the (equilateral) polygonal knot space and an analysis using the HOMFLY polynomial as a surrogate for the topological knot type. As a consequence, one is interested in knowing how large a sample of knots is needed to give a good estimate of the number of topological knot types as detected by distinct HOMFLY polynomials. Some theoretical and experimental efforts concerning this question will be discussed.

Speaker: Enzo **Orlandini** (Universita di Padova)
Title: Topological effects on the dynamics of knotted polymers
Abstract: Knots are frequent in long polymer rings at equilibrium and it is now well established that their presence can affect the static properties of the polymer. On the other hand, topological constraints (knots) influence also the dynamical properties of a polymer. This has been indeed shown in recent experiments where the motion of a single knotted DNA has been followed within a viscous solution and in the presence of a stretching force. These experiments raise interesting challenges to the theoretical understanding of the problem, an issue that is still in its infancy. As a first step towards the understanding of the mechanism underlying the mobility of a knot, we investigate by Monte Carlo simulations the relaxation and diffusion dynamics of flexible knotted rings in equilibrium under good solvent conditions. By focusing on prime knots and using a knot detection algorithm we are able to monitor the diffusion in space of the knotted part of the ring, and observe in time the fluctuations of its length along the backbone. This allows to identify a novel, slow topological timescale, and to show that it is related to a self-reptation of the knotted region. For open chains, knotted configurations do not represent an equilibrium state any more. However, under suitable conditions, (for example very tight knots or quite rigid chains) knotted metastable states persist for a very long time and a statistical description of their dynamical properties is then possible. By performing off lattice molecular dynamic simulations of a semiflexible polymer we estimate the average living time and the stability of these states as a function of the initial conditions (size of the initial knot) and of the rigidity of the chain.

Speaker: Eric **Rawdon** (University of St. Thomas)
Title: *Equilibrium Lengths of Random Equilateral Polygons*
Abstract: We present computer simulations to examine the equilibrium length of random equilateral polygons with respect to different spatial quantities, in particular with respect to the total curvature and total torsion of the polygons. We use Markov Chain Monte Carlo methods to determine likely scaling profiles and error bars for our equilibrium length calculations.

Speaker: Andrew **Rechnitzer** (University of British Columbia)
Title: Mean unknotting times of random knots and embedding
Abstract: We study mean unknotting times of knots and knot embeddings by crossing reversals, in a

problem motivated by DNA entanglement. Using self-avoiding polygons (SAPs) and self-avoiding polygon trails (SAPTs) we prove that the mean unknotting time grows exponentially in the length of the SAPT and at least exponentially with the length of the SAP. The proof uses Kesten's pattern theorem, together with results for mean first-passage times in the two-parameter Ehrenfest urn model. We use the pivot algorithm to generate random SAPTs of up to 3000 steps and calculate the corresponding unknotting times, and find that the mean unknotting time grows very slowly even at moderate lengths. Our methods are quite general---for example the lower bound on the mean unknotting time applies also to Gaussian random polygons. This is work together with Aleks Owcarek and Yao-ban Chan at the University of Melbourne, and Gord Slade at the University of British Columbia.

Speaker: Buks Janse **van Rensburg** (York University)
Title: Squeezing knotted polygons in a slab
Abstract: In this talk I discuss the properties of lattice polygons of fixed knot types in a slab of width w by using scaling arguments and by presenting numerical results from Monte Carlo simulations using the BFACF algorithm. If $p_n(K)$ is the number of polygons of length n and of knot type K in the cubic lattice, then it is known that $\lim\to\infty[\log p_n(Ø)]/n = \log \mu_Ø$ exists, where K = Ø is the unknot, and $\mu_Ø$ is the growth constant of unknotted polygons in the cubic lattice. Suppose that $p_n(K,w)$ is the number of knotted polygons of length n and of knot type K in a slab of width w in the cubic lattice. The generating function of this model is given by $g_K(w; t) = \sum p_n(K,w)\, t^n$, where t is a generating variable conjugate to the length of the polygons. The mean length $\langle n\rangle_{K,w}$ of polygons of knot type K in a slab of width w may be estimated from gK(w; t) using the BFACF algorithm. The dependence of $\langle n\rangle_{K,w}$ on w is estimated for $t = \mu_Ø^{-1}$, and the results are compared to predictions of scaling arguments. In addition, numerical results for the metric properties of knotted polygons in this ensemble will be presented.

Speaker: Jon **Simon** (University of Iowa)
Title: *Measuring tangling in large filament systems*
Abstract: Imagine a protein or other polymer filament (or several) entangled in some complicated way, perhaps with tens or hundreds of crossings. Now imagine a second example with similarly large entanglement. Can we say something useful to distinguish the tangling in the two examples? For relatively small systems, topological knotting and linking is a powerful tool, witness the success of "topological enzymology". But for large systems, calculating exact knotting and linking may be computationally impractical; there are uncertainties in how to deal with open filaments; and knowing that one is knot 10.156 and the other 10.157 might not tell us much about the physical properties of the given system. We propose that describing and quantifying tangling in large filament systems should be one of the important next-stage problems for the field of “physical knots.” To describe shapes of proteins (in static conformations), several researchers have developed numerical descriptors based on variations of Gauss’s linking-number integrals; these are related to average crossing number. We have begun studying another modification of average crossing number that we call the “average bridge number”. This is a simple idea, but when taken together with average crossing number, it seems to distinguish nicely between different kinds of packings for long filaments. And there appears to be reasonable stability of the relationship under random perturbations, so this approach may be useful for statistical ensembles as well as for individual conformations.

Speaker: Christine **Soteros** (University of Saskatchewan)
Title: Asymptotics of Knotting After a Local Strand Passage
Abstract: On the macroscopic scale, circular DNA can be viewed simply as a ring polymer. Experimental evidence indicates that topoisomerases act locally in DNA allowing two strands of the DNA that are close together to pass through one another (i.e. enabling a ``local" strand passage) in order to disentangle the DNA. This has inspired investigation of the following question about self-avoiding polygon (SAP) models: Given a SAP with a fixed knot type, how does the distribution of knots after a local strand passage depend on the initial knot type of the SAP, the length of the SAP, and on the specific details of the strand passage such as where the strand passage occurs and the

number of edges altered in the strand passage? In 2000, graduate student M. Szafron introduced a model of unknotted ring polymers in dilute solution for which it is assumed that two segments of the polymer have already been brought close together for the purposes of performing a local strand passage. The conformations of the ring polymer are represented by n-edge unknotted polygons containing a specific pattern (designed to facilitate a strand passage in which exactly two segments of the polygon pass through each other) on the simple cubic lattice. We assume that each such SAP conformation is equally likely. We have investigated, both theoretically and numerically, the distribution of knots after a strand passage has been performed at the location of the special pattern. In this talk, the theoretical and numerical (via Markov Chain Monte Carlo) results for this model will be reviewed with emphasis on the asymptotic properties as n increases. In addition, results for the extension of the model to other knot types such as the figure-eight knot will be presented.

Speaker: Andrzej **Stasiak** (Universite de Lausanne)
Title: Model of selective simplification of DNA topology by DNA topoisomerases
Abstract: We test the hypothesis that type-2 DNA topoisomerases maintain the steady state level of DNA knotting below the thermodynamic equilibrium by acting as topological filters that recognize preferentially certain geometrical arrangements of juxtaposed segments. We show that such specificity can result in two interrelated topological consequences: maintaining the steady-state knot probability level below the topological equilibrium and selecting a specific way of relaxation of more complex knots. We observe, in addition, that local structures in random configurations of a given knot statistically behave as analogous local structures in ideal geometric configurations of the corresponding knot types.

Speaker: Atillio **Stella** (Universita di Padova)
Title: *Ranking knots of random, globular polymer rings*
Abstract: Issues related to the probability of realization of configurations with specific knots in closed random chains play a major role in topological polymer statistics and in its applications to macromolecular and biological physics. A problem of considerable current interest is that of comparing the knot spectra obtained for random models with those analyzed by electrophoresis for the DNA extracted from viral capsids. This comparison should help in identifying specific mechanisms of knot formation in the biological context. In the case of collapsed polymer rings, interest in the knot spectrum is also enhanced by the recent discovery that knots are fully delocalized along the backbone. Understanding if, and up to what extent, topological invariants can affect the globular state in such conditions is an intriguing fundamental issue. We will present an analysis of extensive Monte Carlo simulations of interacting self-avoiding polygons on cubic lattice. The results show that the frequencies of different knots realized in a random, collapsed polymer ring decrease as a power (about -0.6) of the ranking order. This Zipf type of law also suggests that the total number of different knots realized grows exponentially with the chain length. Relative frequencies of specific knots converge to definite ratios for long chains, because the free energy per monomer, and its leading finite size corrections, do not depend on the ring topology, while a subleading correction only depends on the minimal crossing number of the knots. This topological invariant appears to play a fundamental role in the statistics of collapsed polymers.

Speaker: De Witt **Sumners** (Florida State University)
Title: DNA knots reveal chiral packing of DNA in phage capsids
Abstract: Bacteriophages are viruses that infect bacteria. They pack their double-stranded DNA genomes to near-crystalline density in viral capsids and achieve one of the highest levels of DNA condensation found in nature. Despite numerous studies some essential properties of the packaging geometry of the DNA inside the phage capsid are still unknown. Although viral DNA is linear double-stranded with sticky ends, the linear viral DNA quickly becomes cyclic when removed from the capsid, and for some viral DNA the observed knot probability is an astounding 95%. This talk will discuss comparison of the observed viral knot spectrum with the simulated knot spectrum, concluding that the packing geometry of the DNA inside the capsid is non-random and writhe-directed.

Speaker: Carla **Tesi** (Universita di Bologna)
Title: Knotting probability of polygons under stretching force.
Abstract: Knots are practically unavoidable in long polymer rings and influence their properties. This has been witnessed by an increasing number of experiments that can nowadays probe the detailed properties of knotted molecules. In particular micro-manipulation techniques enable direct measurements of mechanical properties of a single molecule, and it is also possible to probe the behaviour of artificially knotted DNA. It is becoming important to study theoretically how, for example, the presence of topological constraints (knots) can affect the mechanical or elastic responses of knotted molecules under external forces. As a first step in this direction we have considered first the problem of looking at how the entanglement complexity in ring polymers can be affected by the presence of a tensile or contractile force. A possible experimental realization of this problem could be bacterial (or mitochondrial) DNA in solution with topoisomerases that are subjected to an external force (AFM or optical tweezers) or to a flow files (shear flow for example). In this work stretched ring polymers are modelled by polygons in the cubic lattice weighted by a fugacity coupled to its span along a given direction. By performing extensive Monte Carlo simulations on this system we have been able to estimate how the knotting probability and the knot spectra depends on the force strength, both in the extensile and in the contractile regime. These findings have to been compared with recent rigorous results on similar models of stretched polygons.

Speaker: Mariel **Vazquez** (San Francisco State University)
Title: Modelling DNA topology simplification
Abstract: Random cyclization of linear DNA can result in knotted DNA circles. Experiments on DNA confined inside P4 viral capsids have found knotting probabilities as high as 0.95. A full description of the complicated knots remains unavailable. Type II topoisomerases unknot DNA very efficiently by performing strand-passage on DNA strands. Motivated by these biological observations, we study random state transitions in knot space for all prime knots with 8 or fewer crossings and fixed length. Our main goal is to quantify unknotting under different geometrical constraints. Our long-term goal is to understand the mechanism of action of type II topoisomerases, and to characterize the knots extracted from the P4 capsids.

We use the Monte Carlo based BFACF algorithm to generate ensembles of self-avoiding polygons (SAP) in Z^3 with identical knot type and fixed length. The BFACF algorithm produces a reducible Markov chain whose ergodicity classes are the knot types. We perform random strand-passage on these knots, compute state transitions between knot types, and steady-state distributions after repeated strand-passages. Introducing different topological biases results various probability distributions.

The large amount of knots used in our model makes it possible to gather additional information regarding knots and their projections. We compute minimal lattice knots, and in some cases improve existing lower bounds. We also provide other physical measures such as the writhe and average crossing number. Finally, using an algorithm that removes Reidemeister I and II moves simultaneously, we compute the average number of crossings before and after Reidemeister removal.

Speaker: Alexander **Vologodskii** (New York University)
Title: Statistical-Mechanical Analysis of Enzymatic Topological Transformations in DNA Molecules
Abstract: Over the last several years I applied computer simulations of DNA conformations to analyze the action of different enzymes capable to change DNA topology. The goal of this talk is to analyze the approach in general terms. First, I will specify what exactly can be computed by the method, and how the computational results can be used to test a particular model of the enzyme action, used in the simulation. It will be shown how two kinds of experimental data can be compared with the simulation results. I will analyze the major assumptions and theoretical bases of the approach. Then the key elements of the simulation will be briefly considered. This general description of the approach will be illustrated by specific examples.

Speaker: Stuart **Whittington** (University of Toronto
Title: *Random Knotting: what we know and what we think we know*
Abstract: A discussion of "what we know and what we think we know" concerning random knotting. (provided by KCM)

Speaker: Lynn **Zechiedrich** (Baylor College of Medicine)
Title: DNA entanglement and resolution; A matter of life, death, and evolution
Abstract: DNA must be long enough to encode for the complexity of an organism, yet thin and flexible enough to fit within the cell. The combination of these properties greatly favors DNA collisions, which can tangle the DNA. Despite the well-accepted propensity of cellular DNA to collide and react with itself, it is not clear what the physiological consequences are. When cells are broken open, the classified knots have all been found to be the mathematically interesting twist knots. These remarkable knots can have very high knotting node numbers (complexity), but can be untied in only one strand passage event. We used the Hin site-specific recombination system to tie twist knots in plasmids in *E. coli* cells to assess the effect of knots on the function of a gene. Knots block DNA replication and transcription. In addition, knots promote DNA rearrangements at a rate four orders of magnitude higher than an unknotted plasmid. These results show that knots are potentially toxic, and may help drive genetic evolution. The enzymes that untie knots are the type-2 topoisomerases. How they carry out their function to unknot and not knot DNA is largely unknown. Although domains of type-2 topoisomerases have been crystallized and the atomic structures solved, no complete, intact, active enzyme structure is known and no co-crystals with DNA have been obtained. We used electron cryomicroscopy (CryoEM) to generate the first three-dimensional structure of any intact, active type-2 topoisomerase. Our data suggest a simple one-gate mechanism for enzyme function.