07w5095 The Mathematics of Knotting and Linking in Polymer Physics and Molecular Biology

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1 Introduction

The focus of this workshop was the mathematics associated with an array of cutting edge problems in polymer physics and molecular biology showing promise for immediate progress at the interfaces between mathematics and the physical and life sciences.

The first targeted area concerns the presence of knotting of DNA in living cells at a steady-state level lower than the thermodynamic equilibrium expected for a system in which inter-segmental passages within long DNA molecules occurs at random. Can one develop a systematic approach to understanding the wide range of potential topoisomerase mechanisms and their application in diverse settings? Is there a selective topoisomerase mechanism by which knotting is kept below a topological equilibrium or are there specific constraining mechanisms promoting this relaxation of knots? The study of the characteristics of the equilibrium now include geometric, spatial, and topological aspects that may be implicated in these mechanisms as well as the characteristics of polymers, for example under theta conditions. Computational, experimental and theoretical aspects of this area were featured in many of the presentations and discussions.

The second targeted area concerns the mathematical, statistical, and computational tools under development for the study of knotting and linking of open and closed macromolecules. One example is the collection of strategies developed to quantify and characterize the entanglement, e.g. knotting and linking, of open macromolecules which show promise for practical application of

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polymers. Another is the development of different methods for the selection of random equilateral polygons, with respect to the natural measure on the space of equilateral polygons. With efforts to quantify a wide range of new spatial features of these random equilateral polygons, greater care is necessary in order to demonstrate that the selection process is sufficient to provide statistically accurate estimations of critical quantities. Still another concerns the methods used to identify the topological type of the knotted polygons. Many of these methods are based on calculations of the Alexander polynomial or the more recent Jones and HOMFLY polynomials. While these have worked well to date, research questions are now moving into the range of 1500 edges (or Kuhn statistical segments) and, therefore, many thousands of crossings in a generic projection. Still another, distinct, computational thrust concerns efforts to achieve optimal spatial configurations when measured by the ropelength. With effort by several teams, this work faces challenging theoretical and computational obstacles.

The third focus is the application of the theory and methods above to the study of macromolecules in confined geometries, for example polymers between two parallel planes as in models of steric stabilization of dispersions or in DNA molecules contained in a capsid. Macromolecules so confined exhibit significantly different average and individual structures in comparison with those in free environments. Effective confining arises in the case of macromolecules that have specific hydrophobic and hydophilic regions or when regions have restricted flexibility or torsion. While, in general, one might expect that much is now known concerning the knotting of macromolecules in such environments, in fact little is known rigorously and many fundamental questions appear to be beyond immediate reach, both theoretically or via numerical studies.

2 Knotting in DNA and polymers

One of the key themes of this workshop was the focus upon the implications of experimental results in the context of theoretical models to understand them and their physiological implications. Setting the theme, **Lynn Zechiedrich**'s opening session described the role of knotting on gene function by leading to a significant increase in mutation. 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. Zechiedrich's group 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 II topoisomerases. How they carry out their function to unknot and not knot DNA is largely unknown. Although domains of type II 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. Zechiedrich's group used electron cryomicroscopy (CryoEM) to generate the first three-dimensional structure of any intact, active type II topoisomerase. The data suggest a simple one-gate mechanism for enzyme function.

Jennifer Mann described how human topoisomerase II α resolves DNA twist knots in a single step. 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 inter-convert DNA topoisomers to resolve knots. These enzymes pass one DNA helix through another by creating an enzyme-bridged transient break. How type II topoisomerases accomplish their unknotting feat is a central question. 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 which accompany transcription, replication, and segregation, thus increasing the likelihood of DNA damage. The 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. Mann's data show that purified five- and seven-noded twist knots are converted to the unknot by human topoisomerase II α with no appearance of either trefoils or five-noded twist knots which are intermediates if the enzyme acted on one of the inter-wound nodes.

Dorothy Buck presented a topological model that predicts which knots and links are the products of site-specific recombination. Buck described 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. The model relies on only three assumptions and Buck provided biological evidence for each of these assumptions. This talk presented the biological background, evidence, and applications of the model that was further explored in the talk of Erica Flapan. The biological determination is accomplished 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.

Giovanni Dietler reported on the properties of knotted DNA in respect to the critical exponents and the localization of the knot crossings. He showed that probably two universality classes exist in this case and that localization of the knot crossings could explain the activity of the topoisomerases. Gel electrophoresis of DNA knots was discussed and simulations as well as experiments were presented in which the knot complexity and its topology play an essential

role. Some hydrodynamics experiments with knots were presented at the end.

3 Mathematical, statistical, and computational methods

Discussing models employed in modeling DNA molecules, **Alexander Vologodskii** put the attention on the discrete worm-like chain, a carefully tested model that leads to a reliable analysis of enzymatic topological transformations. First, he described 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. He showed how two kinds of experimental data can be compared with the simulation results and discussed the major assumptions and theoretical bases of the approach. Then the key elements of the simulation were briefly considered. This general description of the approach was illustrated by specific examples.

Hue Sun Chan described the statistical mechanics of how recognition of local DNA juxtaposition geometry may underlie the unknotting and decatenating actions of type II topoisomerases. Topoisomerases may unknot and decatenate by recognizing specific DNA juxtapositions. 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, 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 was determined; and it was ascertained how the knot/unknot topology and global linking were altered by a topoisomerase-like segment passage at the juxtaposition. Presented results showed 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, the selective segment passage at hooked juxtapositions can 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 earlier experiments on type II topoisomerases from different organisms, the unknotting potential of a juxtaposition geometry in the presented model correlates almost perfectly with its corresponding decatenation potential. These quantitative findings suggest that it is possible for type II topoisomerases to disentangle by acting selectively on juxtapositions with hook-like geometries.

Andrzej Stasiak presented another perspective on a model of selective simplification of DNA topology by DNA topoisomerases. The presented model tested the hypothesis that type II 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, "hooked relationships". It was shown 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. It was observed, 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.

Mariel Vazquez contributed to the theme of modeling DNA topology simplification. 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, Vazquez and colleagues studied random state transitions in knot space for all prime knots with 8 or fewer crossings and fixed length. The main goal was to quantify unknotting under different geometrical constraints. The long term goal is to understand the mechanism of action of type II topoisomerases, and to characterize the knots extracted from the P4 capsids. They used 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. They performed random strand-passage on these knots, computed state transitions between knot types, and steady-state distributions after repeated strand-passages. Introducing different topological biases resulted in various probability distributions. The large amount of knots used in their model made it possible to gather additional information regarding knots and their projections. They computed minimal lattice knots, and in some cases improve existing lower bounds. They also provided other physical measures such as the writhe and average crossing number. Finally, using an algorithm that removes Reidemeister I and II moves simultaneously, they computed the average number of crossings before and after Reidemeister removal.

Christine Soteros discussed the asymptotics of knotting after a local strand passage. 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 which 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. Based on the assumption that each such SAP conformation is equally likely, Soteros and Szafron investigated, both theoretically and numerically, the distribution of knots after a strand passage has been performed at the location of the special pattern. The talk reviewed the theoretical and numerical (via Markov Chain Monte Carlo) results for this model 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 were presented.

Enzo Orlandini discussed the topological effects of knotting on the dynamics of polymers. 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 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, the relaxation and diffusion dynamics of flexible knotted rings in equilibrium under good solvent conditions was investigated by Monte Carlo simulations. By focusing on prime knots and using a knot detection algorithm it was possible 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 identified a novel, slow topological time-scale, 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, an estimate was obtained of 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.

Carla Tesi discussed the probability of knotting of polygons under a stretching force. 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 behavior 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 Tesi and colleagues 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 experi-

mental 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 flow files (shear flow for example). In this work stretched ring polymers are modeled 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 they 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 were compared with recent rigorous results on similar models of stretched polygons.

Isabel Darcy described the modeling of protein-DNA complexes in three dimensions using TopoICE (Topological Interactive Construction Engine). 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.

Eric Flapan described the topological faces of the model for DNA knotting and linking developed jointly with Dorothy Buck. Flapan presented a topological model that predicts which knots and links can be the products of site-specific recombination. This is done 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. The model relies on only three assumptions and we give biological evidence for each of these assumptions.

Alexander Grosberg described metastable tight knots as a worm-like polymer. Based on an estimate of the knot entropy of a worm-like chain. Grosberg and colleagues 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. The 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 these ideas were proposed.

Bertrand Duplantier discussed random linking of curves and manifolds. Duplantier proposed a formalism for evaluating random linking integrals of closed curves in $\mathbb{R}^3$ or, more generally, manifolds in $\mathbb{R}^n$, 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.

Tetsuo Deguchi discussed the dynamics and statistical mechanics of knotted ring polymers in solution using a simulations approach toward an experimental confirmation of topological effects. Deguchi described how topological effects may give nontrivial results on the macroscopic behavior of ring polymers in solution and how one can confirm them experimentally. Numerical evaluations of some characteristic physical quantities of the solution that can be measured in polymer experiments were presented. This study was strongly motivated by recent experimental developments for synthesizing ring polymers with large molecular weights. Numerical results on dynamical and statistical properties of a dilute solution of ring polymers where topological constraints play a central role were presented. Dynamical quantities such as the diffusion constants of ring polymers in solution and the viscosity of the ring-polymer solution were discussed. These show their difference 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. It was 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 one derives the mean square radius of gyration. It is therefore important to evaluate numerically the scattering function of a knotted ring polymer in solution. Some theoretical and simulational results on the scattering functions were discussed.

Kenneth Millett discussed 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 were discussed.

Rob Kusner discussed the geometric problems for embedded bands in space. Just as one can minimize the ropelength for knotted or linked space curves, one 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, one gets knotted or linked "raceways" in the plane, a flattened analogue of knotted or linked "ropes" in space. Kusner showed that the bandlength of raceways grows at least as fast as the square root of crossing number (recall that for ropes one

had instead the three-fourths power) and that this power is sharp. Kusner also commented on the shapes of length minimizing raceways, and speculated on bands or raceways as models for folded or packed proteins.

Atillio Stella discussed how 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. An analysis of extensive Monte Carlo simulations of interacting self-avoiding polygons on cubic lattice was presented. The results showed 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 of 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.

Jon Simon discussed the problem of measuring tangling in a large filament system. 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 one 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. Simon proposed 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 Gausss linking-number integrals; these are related to average crossing number. Simon has begun studying another modification of average crossing number called the average bridging 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.

Jason Cantarella gave a talk intended 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 introduced this framework, reviewed some older results about the helicity of vector fields (which measures a kind of average linking number of integral curves), outlined some speculative applications to macromolecules, and introduced some work in progress reformulating the helicity of vector fields from a more modern perspective. Cantarella's reformulation of helicity opens the possibility of constructing a family of "generalized helicity" integrals analogous to finite-type invariants for knots.

Claus Ernst gave a 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.

Eric Rawdon presented 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. Rawdon and colleagues use Markov Chain Monte Carlo methods to determine likely scaling profiles and error bars for the equilibrium length calculations

John Maddocks discussed the optimal packing of tubes in $\mathbb{R}^3$ and $\mathbb{S}^3$, contacts sets in $\mathbb{R}^3$, and connections with sedimentation dynamics.

Henryk Gerlach described the optimal packing of curves on S^2, both families of circles and open curves.

Stuart Whittington reviewed some results about lattice models of ring polymers, focusing on rigorous asymptotic results about the knot probability as a function of length, the topological and geometrical entanglement complexity and the relative frequency of occurrence of different link types. He discussed a number of open questions. For instance, we know that the knot probability goes to unity exponentially rapidly as the size of the lattice polygon goes to infinity but we know almost nothing (rigorously) about the constant appearing in the exponential term. Similarly, although we know that all non-trivial link types where both polygons are knotted grow at the same exponential rate, we know nothing about the sub-exponential terms.

4 Macromolecules in confined geometries

Javier Arsuaga discussed the topological considerations of the interphase nucleus. 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. Recently, a model has been proposed for the interface region between territories in which chromosomes overlap and intermingle. This new model naturally raises the question of whether chromosomes are linked or not. Motivated by this problem Arsuaga and colleagues investigated the linking of curves in confined volumes. Arsuaga presented recent results using the uniform random polygon model. First, analytically, they showed that the linking probability between a fixed closed curve and a random polygon of length n increases as $1 - O((\frac{1}{n})^{\frac{1}{2}})$. Next, numerically that the linking probability between two polygons of lengths n and m increase as $1 - O((\frac{1}{nm})^{\frac{1}{2}})$. They extended these results to the case when two polygons have a predetermined overlapping volume (as is the case in experimental observations). Arsuaga concluded with a discussion of potential extensions to other polymer models and biological implications.

Buks Janse van Rensburg discussed the properties of lattice polygons of fixed knot types in a slab of width, w, by using scaling arguments and presented 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 $\lim_{n\to\infty} \frac{[log(p_n(\emptyset))]}{n} = log(\mu_\emptyset)$ exists, where $K = \emptyset$ is the unknot, and $\mu_\emptyset$ 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 $g_K(w;t) = \Sigma p_n(\mathrm{K,w})\ t^n$, where t is a generating variable conjugate to the length of the polygons. The mean length $< n >_{K,w}$ of polygons of knot type K in a slab of width w may be estimated from $g_{K(w;t)}$ using the BFACF algorithm. The dependence of $< n >_{K,w}$ on w was estimated for $t = \mu_\emptyset^{-1}$, and the results were compared to predictions of scaling arguments. In addition, numerical results for the metric properties of knotted polygons in this ensemble were presented.

De Witt Sumners discussed why DNA knots reveal chiral packing of DNA in phage capsids. 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 doublestranded 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%. Sumners discussed 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.

Cristian Micheletti discussed the knotting of ring polymers in confined spaces. Stochastic simulations were used to characterize the knotting distributions of random ring polymers confined in spheres of various radii. The approach was based on the use of multiple Markov chains and reweighting techniques, combined with effective strategies for simplifying the geometrical com-

plexity of ring conformations without altering their knot type. By these means, Micheletti and colleagues extended previous studies and characterized 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 $50 \leq n \leq 450$ they showed 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 $\frac{1}{R}$. The dependence of other geometrical indicators, such as writhe and chirality, in terms of R and n was also characterized. It was found that the writhe distribution broadens as the confining sphere narrows

Yuanan Diao discussed the sampling of large random knots in a confined space. Diao proposed 2-dimensional uniform random polygons as an alternative method of sampling large random knot diagrams. In fact, the 2-dimensional uniform random polygons allow one to sample knot diagrams with large crossing numbers that are diagrammatically prime since one can rigorously prove that the probability that a randomly selected 2D 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 on 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 3D uniform random polygons show that these polygons for complicated knots even when they have relatively small number of vertices.

Andrew Rechnitzer talked about the mean unknotting times of random 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) Rechnitzer and colleagues proved 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. They used the pivot algorithm to generate random SAPTs of up to 3000 steps, calculated the corresponding unknotting times, and found that the mean unknotting time grows very slowly even at moderate lengths. These methods are quite general—for example the lower bound on the mean unknotting time applies also to Gaussian random polygons. This work was accomplished in collaboration with Aleks Owcarek and Yao-ban Chan at the University of Melbourne, and Gord Slade at the University of British Columbia.