

DNA does the twist. And the writhe. A “News and Views” item in the May 13 2004 Nature picked up a preprint posted by Maria Barbi, Julien Mozziconacci and Jean-Marc Victor, all with the CNRS. “In the cells of higher eukaryotes, e.g. animals or plants, meters of DNA are packaged by means of proteins into a nucleus of a few micrometer diameter, providing an extreme level of compaction.” As we know, the nuclear DNA contains a library with all the instructions for making and maintaining a cell. But how does one access an item in a library where all the text is on a single line miles long bunched up into a volume inches in diameter? We know there are enzymes (topoisomerases) that allow one strand of DNA to pass through another, so there is no topological obstruction to moving any particular segment of DNA to where it may be copied. But transcription can take place without topoisomerases. How? Barbi and collaborators studied the way that DNA is coiled. The first two levels of packing result in a chromatin fiber.

“In order to provide the transcription machinery with access to specific genomic regions, the corresponding [chromatin] loop has to be selectively decondensed, via a reversible unwinding process that elongates the fiber.” The CNRS team analyzed the way the differential-geometric quantities “twist” and “writhe” vary in terms of the angles and discovered that there is a unique way to simultaneously vary the α s and the β s so that the fiber elongates isotopically: without changing the linking number of the DNA. The unfolding process is illustrated in the following picture, where it is compared with the non-isotopic stretchings that come from changing the α s and the β s separately.

Understanding the ununderstandable. There’s an essay about the nature of mathematical understanding in the May 25 2004 New York Times Science section. Susan Kruglinski interviewed four prominent popularizers of mathematics to find out how much of “the inconceivable, undetectable, nonexistent and impossible” described by mathematics can possibly be explained to

a general audience.

* Ian Stewart, asked if there exist mathematical concepts that cannot be explained to a general audience: “Oh, yes – possibly most of them.”

* Keith Devlin, speaking of the Hodge Conjecture: “Those equations ... are beyond visualization.”

* Brian Greene defends imperfect metaphors: “The equations that govern a violin string are pretty close to the equations that govern the strings we talk about in string theory. So although the notion of strings is metaphorical, it’s pretty close.” And adds: “I suspect that the overarching aim of every mathematical study can be described, even if you can’t get to the guts.”

In what sense do scientists, including mathematicians, understand their own work?

* John Casti: “Mathematics is an intellectual activity – at a linguistic level, you might say– whose output is very useful in the natural sciences.”

This approach sidesteps the question of math’s connection to reality, so understanding may well be besides the point. Brian Greene has the last word: “Our brains evolved so that we could survive out there in the jungle. Why in the world should a brain develop for the purpose of being at all good at grasping the true underlying nature of reality?”

More about Kepler’s Problem. “In Math, Computers Don’t Lie. Or Do They?” was the headline on Kenneth Chang’s exhaustive treatment of the brouhaha surrounding the publication of Thomas Hales’ 1998 computer-assisted proof of the Kepler sphere-packing conjecture (New York Times, April 6, 2004). [Synopsis: Robert MacPherson, Editor of the Annals of Mathematics where Hales’ proof was submitted, assigned the checking to a large group of referees who spent several years at the task and gave up. Everything they examined was OK, but there was always more. The “Solomon-like” decision of the Annals editors: publish the “theoretical underpinnings,” and leave the com-

puter programs, and their output, to be published elsewhere.] Chang describes the problem (“In the Produce Aisle, a Math Puzzle”) and some of its history, but his main focus is computers, as used in mathematical proof. He interviewed John Conway (“I don’t like them, because you sort of don’t feel you understand what’s going on”) and Larry Wos, who claims that the advantage of computers is their lack of preconceptions: “They can follow paths that are totally counterintuitive.” He also did some research on the natural history of mathematical proof. “Even in traditional proofs, reviewers rarely check every step, instead focusing mostly on the major points. In the end, they either believe the proof or not.” An exemplary piece of journalism about mathematics.

Math is hard! This isn’t Barbie speaking, it’s Keith Devlin, NPR’s “The Math Guy,” and he was delivering the keynote address to 15,000 members of the National Council of Teachers of Mathematics at their annual meeting last month in Philadelphia. His remarks were picked up and disseminated by Joann Loviglio of the Associated Press (April 21, 2004). She paraphrases Devlin: “Our brains aren’t well equipped to grasp those kinds of advanced mathematics” (those kinds include adding fractions and calculus). What the brain does naturally is “counting, algebra, geometry and simple arithmetic.” This “natural mathematics” is contrasted with the “formal mathematics” that many NCTM members are condemned to teach, stuff that “seems counter common sense to our brains.” How did Devlin himself become a math professor at Stanford? “Devlin said it was not until he was a graduate student that he really understood what he was doing. ‘I learned to play the game first ... to manipulate the symbols to get the right answer, and the understanding came later,’ he said.” Like Pascal’s method for attaining faith through prayer. More of Loviglio’s paraphrase: “Maybe formalized math should be taught in a manner similar to the immersion method used for teaching language, in which a teacher just starts speaking in a foreign tongue and students eventually start figuring out what’s being said. But not all students learn language that way - and not all students will master formal mathematics.” The AP feed was posted on the webpage of the State College, PA Centre Daily Times. A webcast of the entire opening session, including Devlin’s address, is available on the NCTM’s website.

Recent math history in the Chronicle. “Math with a Moral” is the title of Robert Osserman’s contribution to “The Chronicle Review” in the April 23 2004 Chronicle of Higher Education. Osserman sets the in-

tellectual stage for the Poincaré conjecture and leads us through the main steps in its resolution. This is large-scale and coarse-grained mathematical history for a general audience, but very skillfully done. Osserman leaps from shoulder to shoulder (Riemann, Poincaré, Thurston) in sketching the flow of ideas from geometry through topology and back to geometry. He has a nice metaphor for Thurston’s geometrization conjecture: “William Thurston’s great contribution was to see a way to systematize all those shapes – to provide a kind of periodic table with which to classify and organize all possibilities, as built up out of components based on the original positively and negatively shaped geometries of Riemann, together with a few other basic types.” Then the more recent developments (Hamilton, Perelman) and the news that Perelman’s published and accepted work has been shown, by Perelman himself, and by Toby Colding (NYU) and William Minicozzi (Johns Hopkins), to be already sufficient to settle the Poincaré conjecture. [According to my sources this may be premature: Perelman’s second paper, necessary for this proof, has still not fully been digested. TP] Perelman’s full proof of the geometrization conjecture is still under examination. The story has two morals: “When faced with a problem that seems intractable, the best strategy is sometimes to formulate what appears to be an even harder problem. By expanding one’s horizons, one may find an unanticipated route that leads to the goal. Second, ... usually mathematics is a highly social activity, with collaboration between two or more individuals the rule rather than the exception. ... Even when an individual takes the last step in solving a problem, the solution invariably depends on elaborate groundwork laid by others ...”

Chaos in Nature. “they have developed a powerful new method to determine from experimental observation of a system whether it is chaotic, and, if it is, what the precise quantitative nature of that chaos is.” Thomas Halsey (ExxonMobil Research) and Mogens Jensen (Niels Bohr Institute) are commenting on recent work of Sam Gratrix and John N. Elgin (Physical Review Letters 92 014101), in a “News and Views” piece in the March 11, 2004 Nature. Halsey and Jensen briefly review the methods currently available for determining if a set is or is not a strange attractor. The criterion is multifractality, but box-counting (“simply reconstruct its trajectory through phase space, cover that trajectory with boxes, measure the amount of time spent in each box, and then determine whether or not the multifractal structure you have computed is consistent with chaos”) is unreliable. A safer method involves periodic trajectories. “Mathematicians know that the strange attractor can actually be constructed from the union

of all periodic trajectories of a system, provided that trajectories of arbitrarily long periods are included ...” This method can be applied to an analytically given dynamical system, for example the Lorenz attractor: “Using an ingenious method to categorize these long trajectories, Gratrix and Elgin have reconstructed in great detail both the Lorenz attractor and its multifractal properties.” For systems in nature, there is rarely time for finding enough trajectories to apply this method. But Grantz and Elgin have developed “a much simpler approach, based on recurrence times” and have shown, by applying it to the Lorenz attractor, that it matches the periodic-trajectory method, and should give reliable diagnoses of chaos. “Because calculations based on recurrence times should be relatively straightforward for experimentalists, and as we now have reason to believe that they will be more reliable than box-counting results, we can confidently await a new series of experimental demonstrations of the chaotic properties of a variety of natural systems.” The title of the piece is “Hurricanes and butterflies.”

Atiyah, Singer in The Boston Globe. “MIT professor wins major international math prize” was the heading on a March 30 2004 “White Coat Notes” item by Scott Allen in the Globe. The story is the award of the 2004 Abel Prize to Isadore Singer (MIT) and Michael Atiyah (now at Edinburgh) for their 40-year-old discovery of the Index Theorem. “The Atiyah-Singer index theorem calculates the number of solutions to complex formulas about nature based on the geometry of surrounding space, an idea that is difficult to explain but amazingly useful in both math and physics.” The wide applicability of the index theorem in physics was referred to by the Norwegian Academy of Science and Letters in their citation, where, as quoted by Allen, they described the work as “instrumental in repairing a rift between the worlds of pure mathematics and theoretical particle physics.” King Harald will present the prize on May 25.

Statistical Topology of Networks. “Superfamilies of Evolved and Designed Networks” appears in Science for March 5, 2004. The authors are a team of 8 scientists in various departments of the Weizmann Institute. The idea is to classify networks by the statistical properties of their local topology, in the case of oriented networks by the statistical significance of each of the 13 possible “direct connected triads”. These correspond to the exactly thirteen ways (up to symmetries of the triangle) of placing forward (F), backward (B)

and double-headed (D) arrows on the three edges of a triangle so that all three vertices are touched:

$$BF, FB, FF, FD, DF, DD, FBB, FFF, \\ DBF, DFB, DFF, DDF, DDD.$$

The statistical significance of a triad compares its frequency of appearance with the way it appears in an ensemble of randomized networks with the same degree sequence as the network under examination. (The degree sequence is the distribution of the variable “number of edges per node”). The authors number the triads from 1 to 13, as listed; the sequence of 13 statistical significances is the significance profile of the network. The authors examine a collection of networks arising in nature (“evolved”) or artificially (“designed”) and find four “superfamilies” of networks with very similar significance profiles. For example word-adjacency networks from various languages (English, French, Spanish, Japanese) all fall in the same superfamily. WWW Hyperlinks between pages on the Notre Dame website, and interpersonal social networks from a variety of contexts, fall in another one. Biological systems involving direct transcription interactions and those involving signal transduction interactions fall in two other, distinct superfamilies; the paper justifies this difference in biological terms.

Perelman in Nature. The January 29 2004 issue contains a piece by Emily Singer entitled “The reluctant celebrity,” about Gregory Perelman and his attack on the Poincaré conjecture. Singer gives a sketch of the problem, including a correct intuitive picture of the 3-sphere. Unfortunately one might get the impression that Poincaré was not able to prove that the 3-sphere is simply connected, but let’s not quibble. The roles of Thurston and Hamilton in beginning and continuing work on the Geometrization Conjecture are well described, as is Hamilton’s Ricci flow program (“a systematic procedure that smooths an object’s surface into a simpler ... shape by spreading its curvature”) and the singularities that obstructed it (“Some parts of the surface may transform faster than others, resulting in a ‘lumpy’ shape”). There are nice quotes from mathematicians who knew Perelman before he embarked on his eight-year quest to iron out Hamilton’s singularities. Jeff Cheeger: “He was already considered extremely brilliant; this was apparent in conversation and on the basis of his work.” But the main focus of the article is the reluctance mentioned in the title. That Perelman does not want to bask in the limelight or accept one of the opulent offers dangled before him by american universities is apparently almost as unfathomable as the mental processes that led to his discoveries.

Love Model Equations. The AAAS annual meeting was in Seattle last month, and the February 13 Seattle Times reported on some of proceedings. A local team of psychologists and applied mathematicians presented no less than a “mathematical formula for marital bliss.” Unfortunately this formula, derived by John Gottman, James Murray, Kristin Swanson and their collaborators, is not an algorithm for achieving bliss. Rather it is a mathematical model of a relationship, based on the analysis of how a couple interacts when arguing, that can predict “with 94 percent accuracy which marriages will last and which will end in divorce.” The model is a set of “coupled” first-order ordinary differential equations. In *LoveModelEquations-2.pdf* (available from the online Seattle Times article) Swanson spells them out:

$$\frac{dx}{dt} = q_1 (x_0 - x) + I_1(y),$$

$$\frac{dy}{dt} = q_2 (y_0 - y) + I_2(x).$$

Here I_1 and I_2 are piecewise linear functions (two different positive slopes, changing at 0) which encode the couple’s argument-interaction behavior. Geometrically speaking, the health of the relationship can be read off from the convexity of I_1 and I_2 . Both close to straight lines gives a “validating style of interaction.” Both are very convex downward in conflict-avoiding couples, very convex upward in volatile couples. We are not told the prognosis for a mixed marriage.

Aromatic Möbius strip. “Synthesis of a Möbius aromatic hydrocarbon” appeared as a letter to Nature, December 18, 2003. There is a “Hückel rule” that constrains the number of carbon atoms in cyclic hydrocarbon compounds: the number of carbon atoms in an uncharged ring (always even) must be of the form $4n + 2$. The most familiar member of this family, benzene, has 6 carbons. The Kiel and Stuttgart-based authors (D. Ajami, O. Oeckler, A. Simon, R. Herges) of this article took up a prediction of E. Heilbronner (1964) that rings of $4n$ molecules could be stable if they had the topology of a Möbius strip. They found an ingenious method for synthesizing a stable, twisted “annulene” with 16 carbon atoms: surgery between an annulus-like 8-carbon aromatic molecule and a cylinder-like one (in this case, tetrahydrodianthracene).

“**Malignant Maths**” is the title of a piece in the January 22 2004 Economist. The subtitle is less threatening: “Mathematical models aid the understanding of cancer.” The focus is on three works appearing in

Discrete and Continuous Dynamical Systems–Series B which is devoting its February issue to the topic.

- Zvia Agur and her colleagues (Institute for Medical BioMathematics, Bene Ataroth, Israel) present a model for the workings of angiogenesis (the process by which a tumour creates its own blood vessels). Dr Agur set up a system of differential equations, where the variables are “the number of cells in a tumour, the concentration of the angiogenetic growth factors within it and the volume of the blood vessels.” Analysis of this system led to “the discovery that there are circumstances in which a tumour oscillates in size, instead of growing steadily,” with clear therapeutic implications.
- Denise Kirschner (University of Michigan) describes her investigations into the use of the immune system to fight tumor growth. A novel treatment, known as small interfering RNA (siRNA) therapy, might suppress the action of a molecule called “transforming growth factor beta” (TGF-beta), which large tumours use to elude the immune system. Dr. Kirchner also uses a differential equation model. Her variables are “the number of immune-system ‘effector cells’ (those that combat tumours), the number of tumour cells, the amount of interleukin-2 (a protein that enhances the body’s ability to fight cancer), and an additional variable to account for the effects of TGF-beta. ... In the model, a daily dose of siRNA over the course of 11 successive days succeeded in counteracting the effects of TGF-beta, and so allowed the immune system to bring the tumour under control.”
- Pep Charusanti and his colleagues (UCLA) investigated the action of Gleevec, a drug used against chronic myeloid leukaemia. Gleevec starves cancer cells by inhibiting their metabolism of ATP. The riddle was why Gleevec was ineffective in a “blast crisis,” the terminal state of the disease. Charusanti’s mathematical model “shows that cells in blast crisis expel the drug too quickly for it to be useful as an ATP-blocker,” giving a direction to look for improvements in the therapy.

The article ends by quoting Richard Feynman: “mathematics is a deep way of describing nature, and any attempt to express nature in philosophical principles, or in seat-of-the-pants mechanical feelings, is not an efficient way.”

Bayesian filters for spam. “Bayesian” may be the new geek buzz-word. Here we have Andrew Cantor in his USA Today Cyberspeak column (December 26, 2003) telling us how “The Reverend Thomas Bayes was an 18th century English mathematician who came up with a theorem for determining the probability of an event based on existing knowledge.” And how “In August 2002, Paul Graham wrote an article called ‘A Plan

for Spam’. He suggested using Bayes’s techniques to identify the probability of a message being spam. Unlike other spam filters, this would be based on the content of messages you already knew were spam.” Cantor mentions some commercial products devised to convert this 18th-century notion into 21st-century cash. Article available online.

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