NewScientist
23 FEBRUARY 2002 No 2331 WEEKLY £2.20 US $3.95

IS IT ALIVE?

HOW A HANDFUL OF WIRES AND BRAIN CELLS HAS SPARKED THE CYBORG REVOLUTION

WHY SLEEP IS A GAME OF CHANCE   CLONING AND THE COPYCAT KITTEN

AH, THE joys of a good night's sleep. Eight hours of blissful, uninterrupted shut-eye. Except it never happens.

None of us just hits the pillow and lies comatose till morning. Even a normal, healthy sleeper will wake up between 15 and 35 times each night. That's not usually a problem. Healthy sleepers hardly notice they've woken up before their bodies pull them back to sleep. But, for some people, trying to sleep is a waking nightmare. As many as 10 per cent of the adult population suffer from more extreme sleep-wake disturbances, which leave them constantly tired.

Compared with other branches of medicine, our understanding of sleep is pretty basic, and treating sleep problems is a slow process. Night after night, at sleep clinics like the one run by Thomas Penzel and Jörg-Hermann Peter at the University of Marburg, researchers record and analyse the sleep habits and the vital signs—such as blood pressure, heart rate, breathing rates and so on—of people with sleep problems, hoping to see something that will help them diagnose a particular ailment.

Occasionally, though, they have a happier task: logging the vital signs of people who sleep soundly. Penzel and Peter used to work out the proportion of the night these healthy sleepers would spend asleep and awake, and use that as a control against which to measure the problems of their patients. But that simple view came to an end a couple of years ago, when Penzel met Plamen Ivanov, a Boston University physicist.

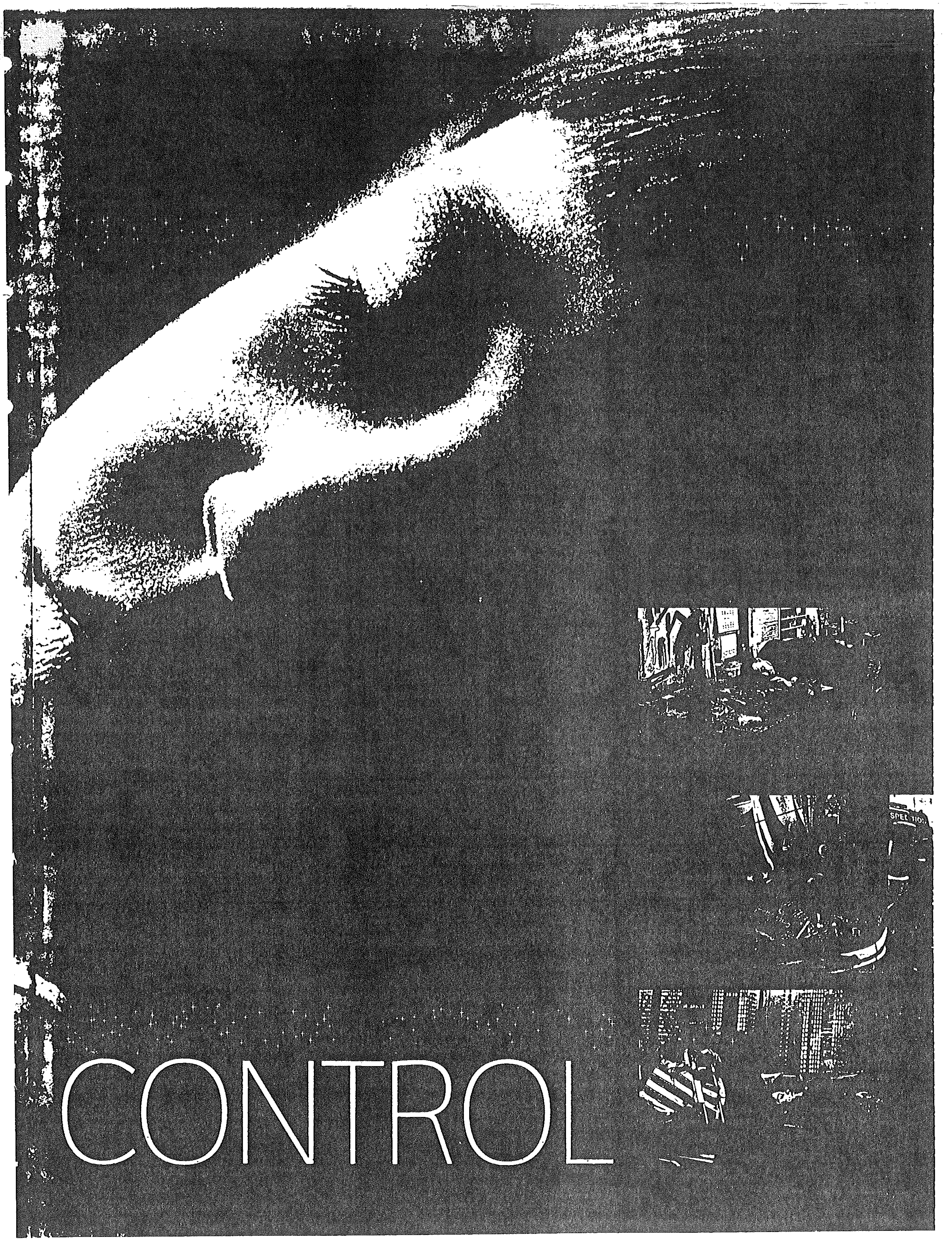
Ivanov works in a research group that has an almost unhealthy obsession with details. Its members are experts in signal analysis, looking for hidden patterns in just about every place they can think of: the heart, the Earth's crust, financial markets. You name it, and they'll find the pattern in its behaviour.

Between them, Ivanov and Penzel began to think there might be undiscovered patterns in the way we sleep at night, and that they might provide a new way of diagnosing and treating sleeping disorders. They and their colleagues have encapsulated these ideas in a paper published in *Europhysics Letters* this month.

To Ivanov, sleep is made up of events whose frequency you can plot mathematically, just as you can plot the severity of earthquakes.

SNOOZE

I. Diguand/Millennium Ginter/Bilderberg/Network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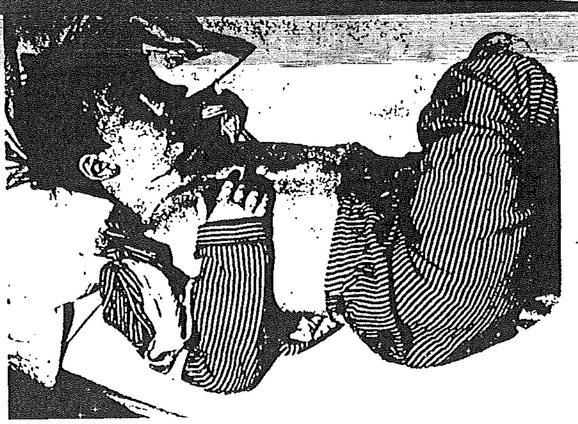

'A STRONGER FORCE PULLS SLEEPERS BACK TO THE LAND OF NOD'

You can take all the earthquakes on the planet for one year, for example, and plot the frequency for each magnitude of earthquake against the magnitude itself. The result is a curve that shows the exact relationship between the size and how often it occurs. With earthquakes, the kind of curve you get is called a power law: the frequency of the quakes falls off in inverse proportion to their magnitude raised to some power. Movements on the stock market behave the same way. But with other phenomena, such as the intervals between signals in human neurons, the frequency decays exponentially instead.

It sounds like an obscure distinction, but it is actually profound. Exponential curves have an inbuilt scale factor: the size jump over which the frequency falls by half is the same no matter where you take your starting point. For power laws this doesn't apply.

This kind of analysis could be just the thing to sort out the problem of a bad night's sleep. Graduate student Chung Chuan Lo got the job of analysing Penzel's sound sleepers. He looked at the length and number of waking periods through the night, and plotted their frequency against how long they lasted. Then he did the same for periods of sleep.

Lo discovered that the waking periods followed a power-law relationship, while the sleep times are exponential. To his colleagues, that was absolutely amazing. In all their years of analysis, the Boston researchers had never before come across a case in which both patterns arise in one system. Normally it's always one or the other. Having discovered this intriguing behaviour, they felt compelled to find out what was at the root of it, and what it might reveal about how sleep works. So they began to build a model.

Scans of brainwave patterns indicate that there are certain distinct sleep states: REM sleep, which usually coincides with dreaming, two other light sleeping states, and two deep states. So they divided the slumber spectrum into a few sleep "microstates". It also seems reasonable that there are many different degrees of waking, from barely conscious to fully alert, so they put a whole set of different waking microstates into the model.

The next stage was based on the latest biological thinking about sleep. A collaboration between Swiss and French neurobiologists published a couple of years ago found that sleep is essentially a battle in the brain between sleep-promoting and wake-inducing neurons (*Nature*, vol 404, p 6781). For their model, the Boston researchers assumed that the result of this complex chemical battle is a kind of random walk: one step towards awake, three steps back towards sleep, another couple of steps back towards wakefulness, and so on in a random pattern.

And that nightly tug of war must be one-sided—a stronger force pulls healthy sleepers back to the land of nod than pulls them awake. So it is common to hit the deepest limit of sleep, but rare that the random walk will fully wake you. "Each time the brain enters the wake state, it is pulled back to sleep quickly," Lo says.

The researchers incorporated all this in an equation and looked to see if it modelled the way people drift in and out of sleep. As they had hoped, it produced the same sleep patterns as the doctors saw in real people—including the all-important mixture of power law and exponential distribution. To the Boston researchers, this is a sign that their model reflects the processes behind sleep.

Night dreaming

But it's not proof. Peretz Lavie, a sleep researcher at Technion in Israel, says that the Boston model is not the only approach that could explain the strange dynamics. He thinks that alternatives might concentrate on the transition from and to REM sleep, which occurs roughly every 90 minutes and is where most of our brief awakenings are clustered.

The Boston team admit that their model is crude and that it will be hard to test the assumptions it's based on, but they still believe it is going to be extremely useful. "It's a toy model," says Ivanov. "But it is the first one to give a rough idea and explanation for a very complex and intriguing phenomenon." And it might have some strange implications.

If sleep really is a random walk, there can be no link between the length of one sleeping period and the length of the waking period that follows. There would also be no correlation between the length of one wake period and the next, or one sleep period and the next. It could explain why you sometimes wake up for no apparent reason, and why people's sleep behaviour is so varied. Light sleepers presumably have too weak a team of sleep neurons. Those who quickly drift off again even after being shaken awake might be blessed with a beefier bunch.

The Boston model is already providing a new set of tools for sleep researchers. The team has looked at sleep apnoea, in which patients have breathing problems that cause them to wake up frequently. Not surprisingly, they saw more short waking periods than normal, but there were also fewer long waking periods. This kind of shift may provide a new way to characterise sleep apnoea, and may also help researchers find out more about how the body responds to such problems. The pattern might indicate, for example, that the sleep neurons tug harder to compensate for the frequent waking.

Back at the Marburg clinic, psychiatrist and neuroscientist Martin Huber is interested in using the analysis to diagnose disorders such as depression that affect moods and feelings. "A disorder of sleep structure is very common in affective disorders," he says. Huber hopes eventually to match different sleep patterns with particular diseases. That might even allow doctors to diagnose diseases before other symptoms show up.

Ivanov is collaborating with Huber to look at how drugs affect sleep patterns. They believe some drugs may limit the number of available wake microstates. It's possible that you may hit your peak wakefulness during a night's sleep, shifting your wake state away from power-law behaviour. Looking for such a shift might provide a way to monitor the side-effects of medications.

All these efforts will, in turn, help refine the Boston researchers' model of sleep. Once a disease or a drug can be linked to a particular sleep pattern, whatever is known about that disease or drug's effects on our bodies should suggest ways to alter the model and faithfully reproduce the altered sleep patterns. As the model improves, it might be possible to see how other, subtle physiological changes affect our sleep.

The researchers are confident they have found an important new path into the relatively unexplored field of sleep. They have certainly made one thing clear: sleep is more than a welcome switch-off at the end of each day. It is a game of chance, a means of diagnosing illness, and a strange new phenomenon in physics. Really, it's enough to keep you awake at night. □

T. Dignand/Hillemann/Ginter/Bilderberg/Network

Mary Dunkin

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*Source: **Boston University (http://www.bu.edu/)***

Date: Posted 6/4/1999

Revealing The Complex Patterns Of Cardiac Disease

Multifractal analysis uncovers differences between healthy and unhealthy hearts

(Boston, Mass.) - In a paper published in Nature this week, scientists from Boston University's Center for Polymer Studies describe a new technique derived from modern physics that can help doctors distinguish between a healthy heart and one that is headed for trouble.

Led by Research Associates Plamen Christov Ivanov and Luis Amaral, the team analyzed the timing of heartbeats of both healthy and sick hearts, looking for fractal patterns - self-similar patterns composed of smaller copies of themselves. They found that healthy hearts exhibited complex multifractal properties, while the beat patterns of unhealthy hearts were monofractal and less varied.

The discovery of the multifractality of the healthy heart is important because current medical practice is to prescribe medication to eliminate variability for patients with irregular heartbeats. "This could be doing as much harm as good," says Professor H. Eugene Stanley, director of the Center for Polymer Studies. Monofractals occur commonly in nature and have long been observed in physiological systems. A fern, for example, is fractal because each frond is composed of sub-fronds, each a miniature, but not necessarily identical copy, of the whole.

Other systems, like the healthy human heart, are much more complex, with dynamic changes occurring periodically over time. An individual jumps up as the alarm rings, pushes the snooze button and dozes for ten minutes, jumps out of bed, downs a cup of coffee and dashes for the bus, then settles in for a slow ride downtown. Each activity results in a different heart rate and the overall system is better described by multifractals - a more complex system of fractals within fractals.

"We presume that the healthy behavior is richer and more complex because it represents the body's ability to adapt to change," says Ivanov. "The ability of the body to adapt to changes in the environment is crucial to survival." The researchers are now working with Mitsubishi of Japan to develop a small monitoring device that would alert the wearer if the heartbeat changes from a multifractal to monofractal pattern. They are also planning to apply this technique to other physiological systems, such as the breathing patterns of people with sleep apnea.

Further information can be found at http://polymer.bu.edu/~amaral/Heart.html

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Note: This story has been adapted from a news release issued by Boston University for journalists and other members of the public. If you wish to quote from any part of this story, please credit Boston University as the original source. You may also wish to include the following link in any citation:
http://www.sciencedaily.com/releases/1999/06/990604081236.htm

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THE LAW IN THE CHAOS : RESEARCHERS IDENTIFY COMMON CHARACTERISTICS OF CLIMATE, STOCK EXCHANGE, AND HEART BEAT

(Seite V2/10/ Sueddeutsche Zeitung Nr. 152, 6 Juli, 1999)

Marcel Ausloss doesn't look like somebody who made a fortune at the stock exchange: the theoretical physicist from the University of Luettich prefers to wear old sweaters and worn up sneakers. All the same Ausloss knows things which would make jealous every stock exchange professional - says he. "Yes, of course", the researcher answers the question, whether he predicted the last stock crash. The colleagues of Ausloos in the Heraeus workshop common characteristics in complex systems taking place in the village of Rauischholzhausen in Hessen were amused, but not too astonished. Some of the believe to be able to do the same. Others prefer speculating on long term weather forecast. Or they speculate on how to predict the risk of heart failure from a human's heart beat.

Such predictions have been considered impossible since the beginning of the sixties. Back then the American meteorologist Edward Lorenz discovered, that the result of weather simulations depends very sensitively on the initial conditions. Lorenz coined found the picture of a butterfly which causes a hurricane by clapping his wings to describe this. Chaos theory was born. One of its main statements: if a system is influenced by many factors in a complicated manner, its future can no longer be computed.

Meanwhile many scientists are more optimistic again: "During the last years we have discovered regularities in many complex systems" says the theoretical physicist Armin Bunde from the university of Giessen. Bunde's group attracted attention last year when the scientists analyzed the up and down of temperature at different weather stations. The result: the weather has the memory of an elephant. When it is warm today this does not only increase the chance of having weather for the beach tomorrow. As well the chance of a warm day in one month or in ten years increases by a small percentage. (SZ, 28.7.98).

So far researchers can only speculate why the weather is so persistent. "Probably the coupling of the atmosphere to the ocean plays a decisive role", speculates Bunde. "The ocean changes its temperatures only slowly". The inert sea could stabilize the moody weather. This explanation is supported by calculations of climate researchers. Jagadish Shukla of the George Mason University in Fairfax simulated winds and precipitation in the tropical region. While he started the simulations with completely different weather data, after some days the different scenarios converged, if the temperature of the surface of the sea was the same. Big cause, small effect - a reversed butterfly picture. "It should be possible to predict the tropical circulation and the amount of rain as long as it is possible to predict the temperature of the ocean", concludes the scientist (Science, vol. 282, p. 728, 1998). That means at least for several months.

Regularities are searched for at the stock exchange as well. Still the daily quivering motion of stock prices is considered unpredictable. Scientists like to compare it to the shivering of particles in a turbulent fluid. "There are however significant connections between certain stocks", says Rosario Mantegna. The Italians physicist from the university of Palermo has compared the fluctuations of different stocks at the New York stock exchange. "One can bundle the stocks into groups with similarly moving prices", reports the physicist. Oil companies for example had similar price histories. His favorite example Mantegna explains by showing a transparency: one can see the prices of Coca Cola and Procter & Gamble moving together for months. "Unfortunately one can't make money from this discovery", complains the Italian. Although for some stocks up and down movements are in parallel, "you never know whether prices will rise of fall".

Another characteristic of stock prices is the change between quiet and turbulent periods. Similar transitions exist in nature as well, for example in the flow of rivers. There one explains the phenomenon with the interaction of billions of molecules. Recently the economist Thomas Lux from the University of Bonn has developed a similar model for the stock exchange (Nature, vol. 397, P. 498, 1999). He explains the transition from the interplay of buyers. Lux divides them into two groups: group one is formed by "fundamentalists" - a species as rational as sluggish. They compose their stock packages according to company data. Group number two are the "noise traders": nervous individuals speculating on fast profits, react to any rumor, and tend to herd behavior. If the noise traders were more successful than their competitors for a while, the fundamentalists may become fickle and change their tactics. The more buyers act on short notice, the more turbulent the stock exchange is.

DETECTING TUMORS

Sceptical Lux is so far to the prophets of stock market crashes. Besides Ausloos Didier Sornette belongs to this group. The solid state physicist from Nizza has scrutinized eight crashes in the period from 1929 until 1998. "Before there is always the same signature", knows Sornette. The price oscillates in shorter and shorter intervals. When the interval becomes zero it crashes as if struck by lightning. A reliable method? "One crash Sornette predicted correctly, with another one he failed", says Lux.

Another type of collapse, the collapse of the heart, investigates physicist Plamen Ivanov from Boston University. Can you read an illness off the heart rhythm? Ivanov has compared the rhythms of healthy and sick people. The latter suffered form heart insufficiency and were in a life threatening condition. Ivanov found clear differences. Sick hearts beat more regularly than healthy ones. Obviously they lost the ability to adapt their power to changing loads. A similar result was found by Gregor Morfill in recent years. The director of the Max Planck Institute for extraterrestric physics in Garching used the scale index method (SIM). The method was originally developed for astrophysics to describe the distribution of galaxies. Morfill's group used it to analyze heart rhythms. The researcher from Munich found characteristic patterns, which indicate an increased risk of heart attack. In this context both a too regular and a too irregular proved dangerous.

In the future SIM shall help diagnosing skin cancer as well. The idea: malign tumors show certain structures, e.g. in their perimeter or in the color distribution. They can be recognized via computer and tumors can be distinguished from harmless spots. "The success rate of computer diagnostics is already as high as that of specialists", says Morfill.

(Translated from German by Dr. Bernd Rosenow, Research Fellow at Physics Department, Harvard University on 22 May, 2000.)

B. Rosenow

Dr.Bernd Rosenow

Robert Tomposki

Robert Tomposki
Notary Public, Commonwealth of Massachusetts
My Commission Expires July 26, 2002

found this article about your work in my newspaper – congratulations.

Das Gesetz im Chaos

Forscher identifizieren Gemeinsamkeiten von Klima- und Börsenentwicklung sowie Herzschlag

Marcel Ausloos sieht nicht aus wie jemand, der an der Börse reich geworden ist: Der theoretische Physiker von der Universität Lüttich trägt am liebsten alte Pullis und ausgetretene Turnschuhe. Trotzdem weiß Ausloos Dinge, um die ihn jeder Börsenprofi beneiden würde – behauptet er. „Ja, natürlich", antwortet der Forscher auf die Frage, ob er den letzten Börsencrash vorhergesehen habe. Die Kollegen von Ausloos auf dem Heraeus-Workshop über Gemeinsamkeiten in komplexen Systemen im hessischen Rauischholzhausen waren belustigt, aber nicht allzu erstaunt. Einige von ihnen glauben, daß sie das auch können. Andere spekulieren lieber über langfristige Wettervorhersagen. Oder darüber, wie man das Risiko für einen Infarkt aus dem Herzschlag eines Menschen ablesen kann.

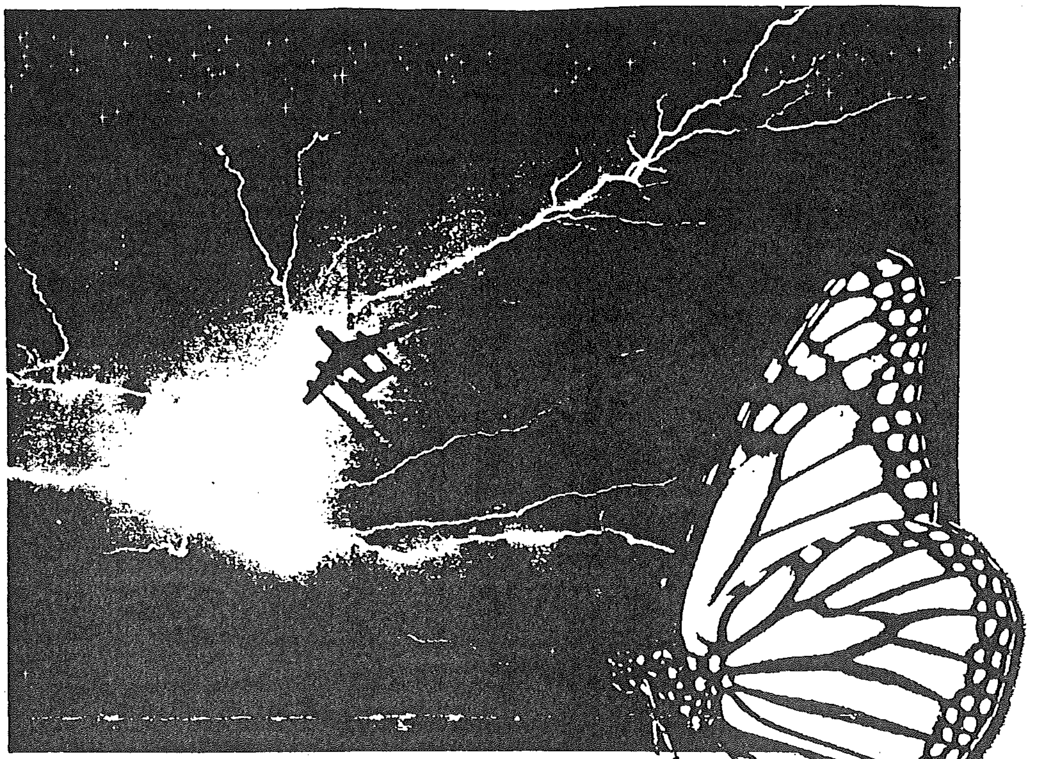
Solche Vorhersagen galten seit Anfang der Sechziger Jahre eigentlich als unmöglich. Damals entdeckte der amerikanische Meteorologe Edward Lorenz bei einer Wettersimulation am Computer, daß das Ergebnis sehr stark von den Anfangsbedingungen abhängt. Lorenz fand dafür das Bild vom Schmetterling, der mit den Flügeln schlägt und so einen Orkan verursacht. Die Chaostheorie war geboren. Eine ihrer Hauptaussagen: Wenn ein System von vielen Faktoren auf komplizierte Weise beeinflußt wird, läßt sich seine Zukunft nicht mehr berechnen.

Inzwischen sind viele Wissenschaftler wieder optimistischer: „Wir haben in den letzten Jahren in vielen komplexen Phänomenen Gesetzmäßigkeiten entdeckt", sagt der theoretische Physiker Armin Bunde von der Universität Gießen. Bundes Gruppe erregte letztes Jahr Aufsehen, als die Wissenschaftler das Auf und Ab der Temperatur an verschiedenen Wetterstationen analysierten. Das Ergebnis: Das Wetter hat geradezu ein Elefanten-Gedächtnis. Wenn es heute warm ist, steigt nicht nur die Chance, morgen Badewetter zu bekommen. Auch ein warmer Tag in einem Monat oder in zehn Jahren wird um einen kleinen Prozentsatz wahrscheinlicher (*SZ*, 28.7.98).

Warum das Wetter so beharrlich ist, können die Forscher bislang nur vermuten: „Wahrscheinlich spielt die Kopplung der Atmosphäre an den Ozean eine Rolle", spekuliert Bunde. „Der verändert seine Temperatur nur langsam". Die trägen Meere könnten das launische Wetter stabilisieren. Die Erklärung wird auch durch Rechnungen von Klimaforschern gestützt. So simulierte Jagadish Shukla von der George Mason Universität in Fairfax die Wind- und Regenverhältnisse in den Tropen. Dabei begann er seine Simulationen mit völlig verschiedenen Wetterwerten. Trotzdem glichen sich die Szenarien binnen einiger Tage an, sofern die Temperatur der Meeresoberfläche gleich war. Große Ursache, kleine Wirkung – ein umgekehrter Schmetterlingseffekt. „Es sollte möglich sein, die tropische Zirkulation und die Regenmenge solange vorherzusagen, wie man die Temperatur des Ozeans vorhersagen kann", folgert der Wissenschaftler (*Science*, Bd. 282, S.728, 1998). Also zumindest über einige Monate.

Gesetzmäßigkeiten suchen Forscher auch an der Börse. Zwar gelten die täglichen Zitterbewegungen der Aktienkurse immer noch als unberechenbar. Wissenschaftler vergleichen sie gern mit dem Gezappel von Teilchen in einer turbulenten Flüssigkeit. „Es gibt aber deutliche Verbindungen zwischen einzelnen Aktien", sagt Rosario Mantegna. Der italienische Physiker von der Universität Palermo hat die Schwankungen verschiedener Werte an der New Yorker Börse verglichen. „Man kann die Aktien zu Gruppen bündeln, deren Kurse sich ähnlich bewegen", berichtet der Physiker. Ölfirmen zum Beispiel hätten ähnliche Kursverläufe. Sein Lieblingsbeispiel belegt Mantegna anhand einer Folie: Darauf sind die Werte von Coca-Cola und des Waschmittelherstellers *Procter & Gamble* zu sehen, wie sie über Monate synchron hin- und herschwankten. „Geld verdienen kann man mit der Erkenntnis leider nicht", klagt der Italiener. Zwar verliefe bei manchen Aktien das Auf- und Ab parallel, „man weiß aber nie, ob sie gemeinsam steigen oder fallen".

Ein weiteres Merkmal von Börsenkursen ist der Wechsel zwischen ruhigen und turbulenten Phasen. Ähnliche Übergänge gibt es auch in der Natur, zum Beispiel bei der Strömung in Flüssen. Dort erklärt man das Phänomen aus der komplizierten Wechselwirkung von Milliarden von Molekülen. Der Wirtschaftswissenschaftler Thomas Lux von der Universität Bonn hat kürzlich ein analoges Modell für die Börse entwickelt (*Nature*, Bd. 397, S. 498, 1999). Er erklärt den Übergang aus dem Zusammenspiel der Käufer. Lux unterteilt sie in zwei Gruppen: Gruppe eins bilden die „Fundamentalisten" – eine ebenso rationale wie träge Spezies. Sie stellen ihr Aktienpaket nach Unternehmensdaten zusammen. Gruppe zwei sind die „Noise-Traders": nervöse Individuen, die auf den schnellen Gewinn spekulieren, auf jedes Gerücht reagieren und zum Herdentrieb neigen. Waren etwa die Noise-Traders eine Zeitlang erfolgreicher als ihre Mitspieler, könnten die Fundamentalisten wankelmütig werden und ihre Taktik ändern. Je mehr Käufer aber kurzfristig agieren, desto turbulenter geht es an der Börse zu.



DER FLÜGELSCHLAG *eines Schmetterlings kann letzlich einen Orkan verursachen. Diese Idee veröffentlichte Anfang der Sechziger Jahre der amerikanische Meteorologe Edward Lorenz.* Photos: M.Prugger/Archiv

Aufspüren von Tumoren

Skeptisch ist Lux bislang gegenüber den Propheten von Börsencrashs. Neben Ausloos gehört dazu beispielsweise Didier Sornette. Der Festkörperphysiker aus Nizza hat acht Zusammenbrüche im Zeitraum zwischen 1929 und 1998 unter die Lupe genommen. „Vorher tritt immer die gleiche Signatur auf", weiß Sornette. Der Kurs schwappe in immer kürzeren Wellen nach oben. Wenn der Abstand verschwinde, stürze er ab wie vom Blitz getroffen. Eine zuverlässige Methode? „Einen Crash hat Sornette richtig vorhergesagt, einmal lag er daneben", sagt Lux.

Eine andere Art von Kollaps, den des Herzens, untersucht der Physiker Plamen Ivanov von der Universität Boston. Kann man aus dem Herzrhythmus eine Krankheit ablesen? Ivanov hat die Rhythmen bei gesunden und kranken Menschen verglichen. Letztere litten unter Herzinsuffizienz und befanden sich in lebensgefährlichem Zustand. Ivanov fand deutliche Unterschiede: Kranke Herzen pochen starrer als gesunde. Offenbar haben sie die Fähigkeit verloren, ihre Arbeitsleistung auf wechselnde Belastungen einzustellen. Zu ähnlichen Ergebnissen war in den letzten Jahren auch Gregor Morfill gekommen. Der Direktor des Max-Planck-Instituts für extraterrestrische Physik in Garching verwendete die Skalierungs-Index-Methode (SIM). Das Verfahren wurde ursprünglich für die Astrophysik entwickelt, um die Verteilung von Galaxien zu beschreiben. Morfills Gruppe analysierte damit Herzrhythmen. Die Münchner Forscher fanden charakteristische Muster, die ein erhöhtes Infarktrisiko anzeigen. Dabei erwies sich sowohl ein allzu starrer als auch ein sehr unregelmäßiger Herzschlag als gefährlich.

In Zukunft soll mit SIM auch Hautkrebs erkannt werden. Die Idee: Bösartige Tumore zeigen bestimmte Strukturen, etwa im Umriß oder in der Farbverteilung. Per Computer könnten diese erkannt und Tumore von harmlosen Flekken unterschieden werden. „Die Trefferquote der Computerdiagnose ist schon genauso gut wie die von Spezialisten", sagt Morfill.

Stefan Greschik

Wenn die Schulter die Finger bewegt

Durch die Implantation einer Neuroprothese kann erstmals ein Patient seine gelähmte Hand wieder benutzen

Ein Sprengstoff-Unfall vor zwei Jahren kostete den damals ...

Im Februar diesen Jahres wurde erst- ...

te zum ersten Mal wieder alleine essen." ...

macher überträgt. Dieser leitet die Signale über die Leitungen und Elektroden an ...

KOMM

Schütz von Biotechni

Der Dachverb schen Biotec (EuropaBio) forde nehmigungsbehö nisch veränderte fall, daß ausgere nach einer Superl Wohl kaum. Die hofft, mit der Refo den europäischen nehmigungsverfa gen zu können. S gen zahlreiche auf Eis. Nur zu ger men auf „Wettbe Arbeitsplatzverlu der Tat: Jeder ver lert den Gewinn d Bei der jetztigen Entscheidung von hörden ab und vo der EU-Staaten, dem Markt komm sich, die Zulassun schärfen und ein zeichnung für G schreiben. Zudem kraftsetzung eine über die Freiset veränderter Orga en Zulassungen f teilt. Die Superbe licher Vorstoß de strie, ihre Interess bild ist die Europ telagentur, die fü Zulassung von M Mit einer ähnlich tution könnten di kehrsfähigkeit" i sehr schnell auf d nenmarkt erreich Die EU-Staaten nicht bereit, zugu behörde ihre Kom ben – aus der Sor Umwelt. Denn and menten, die seit forscht werden, is ne relativ junge D ken, die genmani men und Produk sich noch nicht i abschätzen. So ka Schmetterlingsra wurden für eine S stimmten Gen-M Es ist also von Vor falt an Kontroll- in Europa erhalte

Johanniskraut

Extrakt hemmt r

Johanniskraut-Ex gend hohen Dosieru sionen – das bestätig tersuchungen. Der auch seit langem in folgreich bei Verw nungen und schme krankungen (Neu Christoph Schempp versitätsklinik in Fr aus, warum das Kra ringe Mengen des i enthaltenen Wirksto men das Wachstum *Lancet*, Bd. 353, S. Wegen der äußers des Stoffes Hyperfo nur zwei Untersuchu bielle Wirksamkeit. Extrakt vor allem a reits gegen häufig ei ka resistent sind

CERN COURIER

May 1, 2003

Researchers reveal prime predictability

An interesting discovery may be imminent regarding whether prime numbers appear randomly in the sequence of whole numbers. It has not yet been shown that the occurrence of prime numbers - 2, 3, 5, 7, 11, 13, etc - follows a pattern, or that there is definitely no pattern. Now Pradeep Kumar and colleagues at Boston University have found that the increments in the distances between consecutive primes are not random, but have some rudimentary predictability. For the first few primes the distances are 1, 2, 2, 4 and 2 and the increments are +1, 0, +2 and -2.

The researchers find for example that positive values are almost every time followed by corresponding negative values. These studies, the researchers say, may have consequences for understanding patterns in nature that depend on prime numbers.

Further reading

Nature Science Update www.nature.com/nsu/030317/030317-13.html.

P Kumar, P C Ivanov and H E Stanley Information entropy and correlations in prime numbers http://xxx.lanl.gov/abs/cond-mat/0303110 (2003).

Heartbeat linked to body clock

Study finds erraticpatterns in morning

By Guy Gugliotta / The Washington Post
January 4, 2005

Scientists have long known that more heart attacks occur at midmorning than any other time of day, and while they are not sure why this happens, new research shows that the human "body clock" influences heartbeat patterns, which become more erratic between 9 and 11 a.m.

Reporting in last week's Proceedings of the National Academy of Sciences, researchers from Boston University, Harvard Medical School and Boston's Brigham and Women's Hospital found that "interbeat intervals"- the length of time between successive heartbeats - in five healthy individuals most closely resembled the variability of heart disease patients during the forenoon hours.

Physiologist Steven Shea, of Harvard Medical School and Brigham and Women's Hospital, said the team isolated its five subjects in a dimly lighted, windowless environment for 10 days, varying sleeping patterns and other behaviors so that they could not "signal"the body's internal circadian clock.

Left to fend for itself, each individual's body clock operated on a 24.2-hour cycle, marked by regular changes in body temperature - lowest around 5 a.m. Beginning around 9 a.m., the team noticed significant fluctuations in the heartbeat pattern.

"We're not quite sure why this happens, but it seems to be a transition period during the day," Shea said in a telephone interview.

By GUY GUGLIOTTA

The Washington Post

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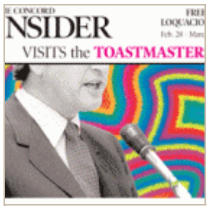

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Преди седмица президентът Георги Първанов си пожела повече американски инвестиции, а Джордж Буш му отговори с настояване за повече реформи и призова: „Където видите корупция, да я изкоренявате.“

Зависимостта между прозрачността на управлението и потока чужди инвестиции, икономическия растеж и жизнения стандарт в една държава е наблюдавана отдавна, но по-скоро не аналитично, а количествено. Проблемът, разбира се, е как да се измери корупцията, която по дефиниция е скрита. Четирима изследователи от Центъра по полимерни изследвания на Бостънския университет - Пламен Иванов (ст.н.с. към Института по физика на твърдото тяло към БАН), Юджийн Стенли - професор по физика, доцент Борис Подобник (от Загребското училище по икономика и мениджмънт, Хърватия) и Джия Шао, докторант, са установили математическа зависимост, която позволява да се определи очакваното ниво на корупция и така да се оцени дали равнището ѝ в дадена държава е повече или по-малко от средното*.

Формулата

Авторите анализират данните на различни страни за брутния вътрешен продукт (БВП) на глава от населението, събирани от Международния валутен фонд, и ги сравняват с индекса за възприятие на корупцията (КИ), определян всяка година от неправителствената организация „Трансперънси интернешънъл“. Този индекс се изчислява на базата на независими изследвания на повече от десет международни институции чрез консултации с местни и чужди анализатори и експерти и социологически проучвания сред гражданите и бизнеса. В индекса, обхващащ 163 страни, най-ниското ниво на корупция се обозначава с 10, а 1 е за най-високото.

Като съпоставят данните за корупционния индекс и БВП, четиримата учени установяват, че има повтаряща се и стабилна корелация между тези две величини. Съотношението между тях се подчинява на степенен закон и може да се опише от формулата

$$КИ \sim (БВП)^n$$

Тоест корупционният индекс е пропорционален на стойността на БВП на глава от населението на степен n.

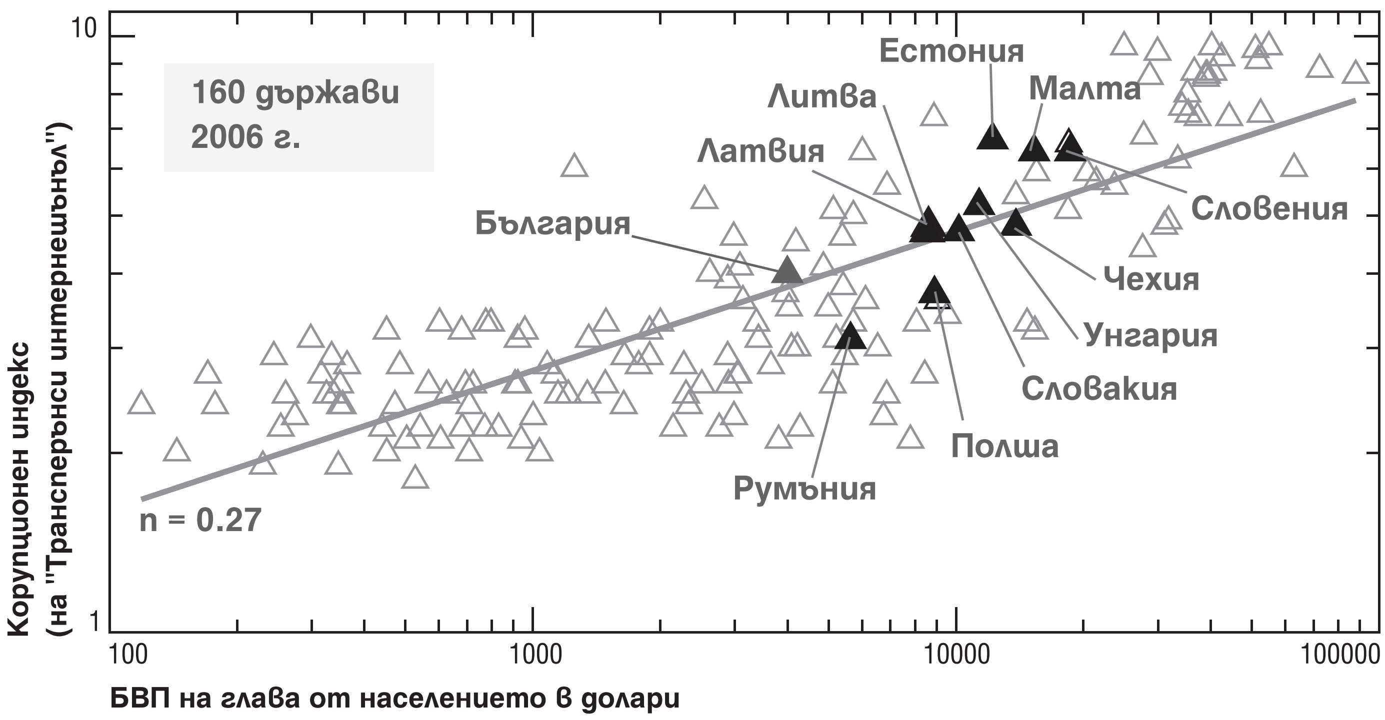
Екипът проектира данните на различен брой страни - между 90 и 155 за периода 2001-2005 г., и установява, че средната стойност на величината n е сравнително стабилна - 0.27, като варира между 0.29 и 0.24. Тази средна стойност те наричат очаквана степен на корупция. (Виж графиката.)

Така истински корумпирани са страните, в които не просто корупционният индекс е висок, а съотношението между него и БВП излиза извън рамките на очакваната степен на корупция. Това позволява да се сравнява корупцията в страни с различна икономическа активност, подчертават авторите на изследването.

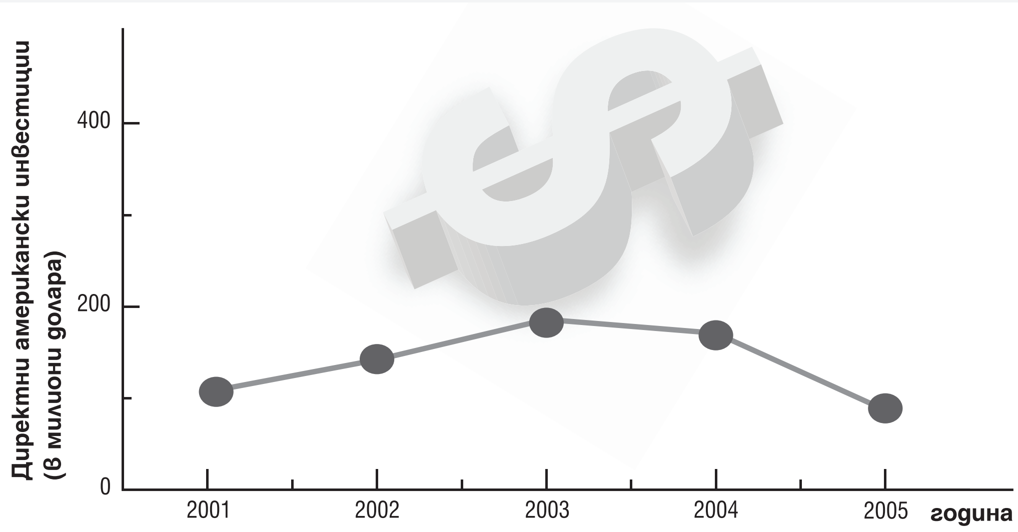
Пред „Дневник“ доктор Пламен Иванов обяснява: „Ние така или иначе предполагахме, че има връзка между икономика и корупция. Дори ако попитате някого на улицата в България, и той ще ви каже, че в по-бедните държави корупцията е по-висока. Новото тук е, че въвеждаме количествен измерител на тази връзка. Вече можем с висока степен на точност да сравняваме корупцията между две страни със сходен доход на глава от населението, както и такива, които имат много нисък и много висок БВП.“

Доказателството

Тази зависимост изглежда универсална за всички държави независимо от социалната система, доходите, географското положение и типа икономика, казва доктор Иванов. Екипът на Бостънския университет е тествал многократно формулата с различни показатели. „Изследвахме различни подмножества от държави. Проверихме данните и за различни години в интервала 2001-2005 г. и дори назад - от 1990 до 2000 г. Анализираме държави с доход до 800 долара на глава от населението или такива с 20 000 долара. Формулираната зависимост се запазва стабилна“, обобщават авторите на доклада. По-важното е, че съотношението е вярно дори когато корупционният индекс на „Трансперънси интернешънъл“ се замени с данните от индекса на корупция, изчисляван от Световната банка. Формулата работи независимо какви методи се използват, за да се мери корупцията, подчертават авторите.



Количественото отношение между Корупционния индекс и БВП на глава от населението е представено с линията, пресичаща графиката. Тя показва очакваното ниво на корупция. Страните над линията са по-прозрачни, а тези под нея - по-корумпирани. България се намира много близо до очакваното ниво на корупция



Американските инвестиции в България за последните пет години

ЧЕТИРИМА УЧЕНИ ОГЛАСИХА ФОРМУЛА, която показва математическата зависимост между нивото на корупцията и качеството на живота в дадена страна. Тя позволява да се въведе количествена оценка на корупцията и доказва емпиричното наблюдение, че колкото по-бедна е една страна, толкова по-корумпирана е тя, толкова по-нисък е икономическият ѝ растеж и чуждестранните инвестиции. Според един от авторите, ако корупцията в България се намали само с 2.5 на сто, доходите на всеки гражданин могат да се повишат с 800 долара на година.

Пламен Иванов прогнозира, че вероятно ще има много хора, настроени скептично към откритието, особено от средите на икономистите. „Все пак изглежда така - явяват се едни физици и предлагат някаква формула, която да отговори на въпрос, отдавна дебатиран в икономическите среди“, казва той. И веднага подчертава, че в съвременната наука зоните на интерес на отделните клонове често се сливат и дори припокриват. Според него това вероятно не е последната дума по въпроса, а само първата стъпка от дебата.

Изводите

„Съотношението ясно показва, че колкото по-корумпирана е една държава, толкова по-бедна е тя. Или това, че бедните държави са непрозрачни. Все още не знаем кой от тези два фактора е първичният“, тълкува резултатите Пламен Иванов.

Изследването извежда също математически, че страни с висока корупция имат нисък, дори незначителен икономически растеж. Пряката зависимост между прозрачност и икономически ръст остава валидна за различни времеви периоди.

Екипът на Бостънския университет установява и силна зависимост между нивото на корупция и чуждите инвестиции. Авторите използват в изследването си данните за американските инвестиции в други страни с мотива, че САЩ са сред основните източници на чужди инвестиции и че американският закон държи инвеститорите отговорни за участие в корупционни практики в чужбина.

По-слабо корумпираните страни от различни континенти са получили повече американски инвестиции на глава от населението от по-непрозрачните, отчитат анализаторите. Според данните им тази пропорция е независима от конкретното ниво на корупция или от БВП на конкретната държава.

Къде е България

Според анализираните данни корупцията в България не е далеч от очакваното ниво. Сравнена с други източноевропейски страни например, България е значително по-прозрачна от Румъния или Полша.

Според доктор Иванов обаче най-важният извод от изследването е възможността да се измерва пряко икономическият ефект от непрозрачното управление. „Докато слушаме политически дебати на тази тема, корупцията си остава абстрактно понятие. След като сме установили пряка математическа зависимост, можем буквално да изчислим цената на корупцията. За България например ограничаването ѝ само с 2.5 процента ще се отрази с повишаване на доходите на всеки гражданин с около 800 долара повече в края на годината. Така темата става съвсем лична, а не абстрактна“, обобщава Иванов. По думите му, ако българинът осъзнае тази връзка, той ще е много по-непримирим към корупцията в каквато и форма да е тя.

Дневник

** Изследването е публикувано в THE EUROPEAN PHYSICAL JOURNAL B, том 56, стр. 157 - 166 (2007) под заглавие Quantitative relations between corruption and economic factors („Количествени отношения между корупцията и икономическите фактори“)*

News | More Science

Heart Rhythms Seem Circadian in Nature

By Sarah Graham | December 21, 2004

The chances of suffering heart problems are not equal throughout the day. Heart attacks occur more often around 10 o'clock in the morning than any other time, a peak that previously was attributed to daily behavior patterns getting underway. A report published online this week by the *Proceedings of the National Academy of Sciences* indicates that the heartbeats of healthy people, too, exhibit strong circadian rhythms, which could help explain the morning crest of adverse cardiac events.

Image:

Steven A. Shea of Harvard Medical School and his colleagues studied healthy individuals between the ages of 20 and 33 years old. The volunteers lived in individual suites for 10 days and had their regular daily patterns disrupted. They were monitored closely and asked to adhere to specific sleep and wake cycles while having their heartbeats monitored using electrocardiograms. The team discovered that a feature of the subjects' heartbeats known as the scaling exponent, which is a statistical classification of beats over time, displayed a significant 24-hour rhythm regardless of daily activities. What is more, the peak occurred between nine and 11 a.m.

According to the report, the findings suggest that "the underlying mechanism of cardiac regulation is strongly influenced by the endogenous circadian pacemaker." And because higher scaling exponents are associated with heart disease, the scientists posit that this fundamental pattern could influence vulnerable people, such as those suffering from congestive heart failure, and contribute to the pattern of early morning heart attacks observed in epidemiological studies.

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New Scientist

Your heart is being closely watched while you're asleep

IF YOU thought sleep is when you really relax, think again. Scientists have discovered that the heart comes under especially close control during sleep. Their findings suggest that sleep may play a role that until now has remained hidden.

Scientists now know that the heartbeat is far more complex and irregular than once supposed (New Scientist, 3 January 1998, p 20). The signals that control a healthy heartbeat contain many different frequency components, and this leads to a highly complex pattern of intervals between beats.

The gaps between heartbeats are "anti-correlated": if the heart speeds up over a short sequence of beats, it will slow down again over the next few beats. More importantly, the pattern of these speed-up/slow-down events can be seen on both short and long timescales: it looks the same over a few beats as it does for a thousand beats. In other words, the heartbeat has a fractal pattern.

An international team led by Plamen Ivanov of the physics department at Boston University decided to compare how the fluctuations in the interval between beats varied between day and night. The results surprised them: during the supposedly relaxed state of sleep, the intervals between heartbeats fluctuated much more strongly, but were brought under control more quickly, showing that the heart is under much closer control during sleep. "It was totally counterintuitive," says Ivanov.

The team initially thought the difference might come about because the body is resting during sleep. Physical activity tends to cause changes in the heartbeat, which would lead to more fluctuations and give the appearance that the heart had less control. But a marked difference remained even when these external influences were taken into account.

The researchers then compared their results with heart data from the cos-monauts on Mir. "It was interesting to compare them with the cosmonauts who were doing something different under different conditions," says Luis Amaral of the Boston team. "But we still got the same results, so this is definitely picking up something intrinsic."

In people with heart disease, the heart is under weaker control than in healthy people. But the researchers found that even heart patients showed an increased level of control when they were asleep.

The results suggest that there might be different mechanisms controlling the heart during waking and sleep, hinting at a hitherto unsuspected role for sleep. "I can't tell you what sleep means," says Harvard cardiologist Aryl Goldberger, "but maybe a function of sleep is to readjust the heart by exercising the system."

###

Author:Jens Thomas New Scientist magazine issue 4th Dec. 99 Source: Europhysics Journal (vol 48, p 594)

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American Physical Society

Mysterious ways of the heart

New understanding may lead to earlier diagnoses

Despite its seemingly methodical "thump, thump, thump," the heart's rhythm is as complex as a potential lover's intentions on Valentine's Day.

New research, to be reported in the American Physical Society's peer-reviewed journal Physical Review Letters, seems to show that variety may not only add vitality to a budding romance, but the heart as well. Further, the scientists say they have developed a simple computer algorithm that can help decipher the heart's complexity and use it to distinguish between diseased and healthy hearts.

Under normal conditions, timing between heartbeats changes instant to instant in a seemingly random way. Actually, though, scientists are finding those beats have patterns within patterns - some lasting thousands of beats. Yes, the heart has a memory - as long as it's not broken.

"We have found that heart rate changes have a complicated clustering pattern in healthy people, but that pattern tends to break down - sometimes actually becoming too regular - in people with heart failure," says lead author physicist Yosef Ashkenazy, Ph.D. of Boston University.

"These measurements can be easily taken from clinical data," adds co-author Plamen Ivanov, Ph.D. also at Boston University. "This suggests the possibility of aiding bedside diagnosis and prognosis."

In fact, according to Ashkenazy, one of the simplest measurements may provide the most promise for improving diagnosis. Just recording when the heart rate dances up and down between each beat, is enough information to plug into their algorithm.

The scientists are actually reading between the beats. "A typical EKG records how things change over time using average values. Instant to instant changes are blurred out," says cardiologist Ary L. Goldberger, M.D. of Beth Israel Deaconess Medical Center/Harvard Medical School. "Our study takes advantage of recent explorations into finding hidden information from the beat-to-beat dynamics."

The study involved 18 healthy people and 12 with congestive heart failure, looking at about 30,000 successive heartbeats for each of the 30 subjects. Their method showed a stark contrast between the two groups. The data came from the National Institutes of Health's new Research Resource for Complex Physiological Signals database (www.physionet.org). The researchers, who are now looking at larger databases, say they will also post details of their code for other scientists to use at that web site.

In any event, it seems clear that if your Valentine makes your heart dance a bit, it may be more than romantic. It might actually be healthy.

###

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In brief: Disorderly conduct

In a perfectly ordered crystal, electrons exist in a continuum of states whose individual wavefunctions extend throughout the lattice — a consequence of the crystal's long-range order. The introduction of disorder into the system can cause some of the electrons to become localized to individual atoms, and in a one-dimensional system this localization is absolute. But it now seems that if the disorder itself is correlated over a long range, some extended behaviour can re-emerge.

letters to nature

Metal-insulator transition in chains with correlated disorder

PEDRO CARPENA, PEDRO BERNAOLA-GALV�N, PLAMEN CH. IVANOV & H. EUGENE STANLEY

According to Bloch's theorem, electronic wavefunctions in perfectly ordered crystals are extended, which implies that the probability of finding an electron is the same over the entire crystal. Such extended states can lead to metallic behaviour. But when disorder is introduced in the crystal, electron states can become localized, and the system can undergo a metal-insulator transition (also known as an Anderson transition). Here we theoretically investigate the effect on the physical properties of the electron wavefunctions of introducing long-range correlations in the disorder in one-dimensional binary solids, and find a correlation-induced metal-insulation transition. We perform numerical simulations using a one-dimensional tight-binding model, and find a threshold value for the exponent characterizing the long-range correlations of the system. Above this threshold, and in the thermodynamic limit, the system behaves as a conductor within a broad energy band; below threshold, the system behaves as an insulator. We discuss the possible relevance of this result for electronic transport in DNA, which displays long-range correlations and has recently been reported to be a one-dimensional disordered conductor.

Nature **418,** 955–959 (29 August 2002)

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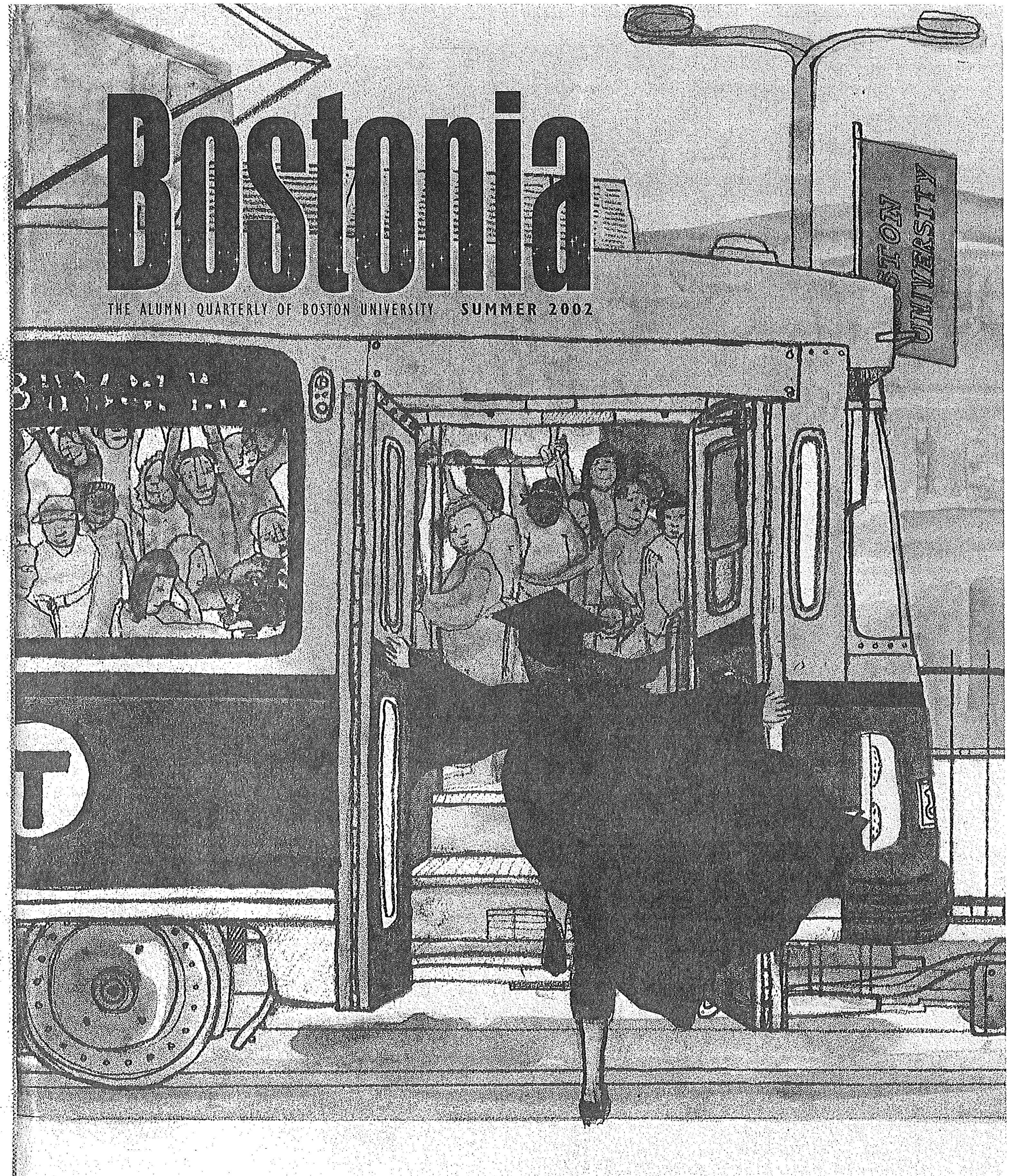
Bostonia

THE ALUMNI QUARTERLY OF BOSTON UNIVERSITY SUMMER 2002



The Arcane Art of Harold Tovish • Choice Mission for NY Timesman as a member of a group than on its own. This suggests that either social interactions boost a termite's immune system, or that the insects are so socially dependent that even brief separation from the parent colony weakens their immune response.

These findings won't console homeowners in the midst of a termite infestation. But for biologists, this work is initiating a new way of thinking about the role of diseases in the evolution of sociality. In his 1971 book *The Insect Societies*, Edward O. Wilson noted that a major cost to group living is that diseases spread easily. Traniello and Rosengaus have found, however, that diseases are not just a cost to sociality; the threat of infection has actually favored the evolution of communication, mutual grooming, biochemical protection, and the exchange of immunity in termites.

"I think that the whole idea of the role that disease plays in the evolution of sociality can be rethought now," Traniello says. "If you're a member of a group, you're at an enhanced risk of an infection, but what we're showing is that it's much more rich than that — that, in fact, social groups can do things to deal with disease that were unimaginable." — *Tim Stoddard*

Bring on the Sandman

BU Physicists Find Odd Patterns in Sleep

DID YOU SLEEP like a baby last night? Probably, even if you don't think of it that way. Most babies actually wake up in fits and starts, and either quickly roll over and go back to sleep, or start yelling for mom or dad. Rather like the rest of us: we might not remember it the next morning, but the average healthy person wakes between fifteen and thirty-five times a night.

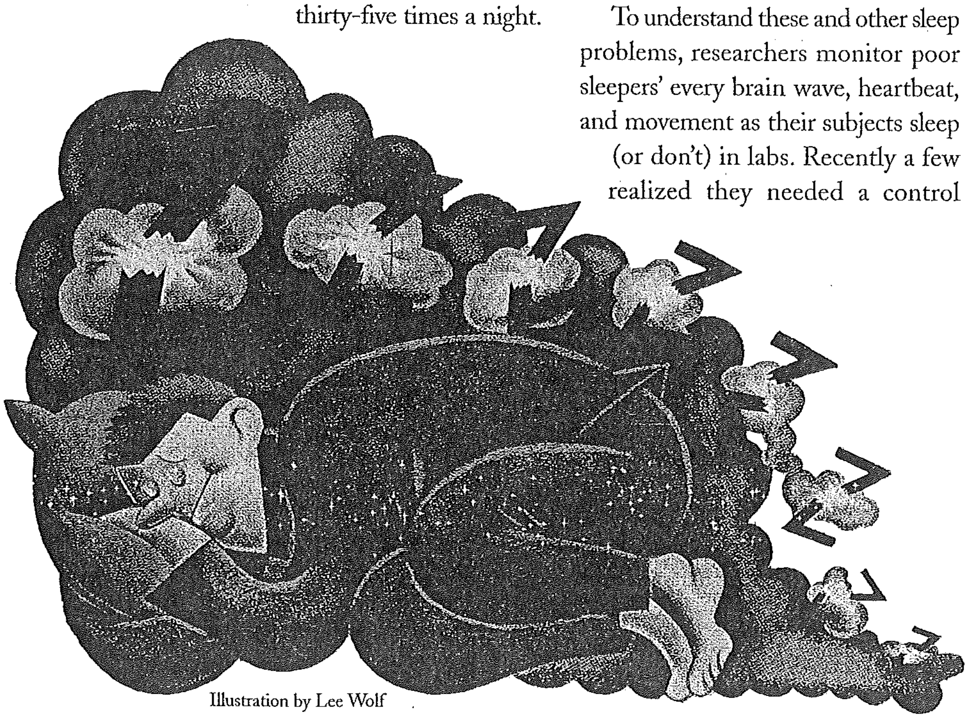


Illustration by Lee Wolf

Researchers have found a struggle between sleep-inducing neurons and wake-inducing neurons during those waking periods, with sleep usually dominating until dawn. So mostly we just roll over and head back to dreamland. But light sleepers have virile wake-inducing neurons and spend more time awake.

To understand these and other sleep problems, researchers monitor poor sleepers' every brain wave, heartbeat, and movement as their subjects sleep (or don't) in labs. Recently a few realized they needed a control study of healthy sleepers. But surprise: the sound sleepers were not sleeping soundly. When the healthy sleepers rolled over, technically they were awake: electrodes attached to their heads in sleep labs sent signals just like those when they were awake.

These data intrigue more than sleep researchers. Searching for patterns hidden in natural and man-made systems, from earthquakes to heartbeats to financial markets, is almost an obsession for a group of BU physicists — theirs is a specialty called statistical physics. Graduate student Chung Chuan Lo *(GRS'04)* and his colleagues at the Center for Polymer Studies were surprised by what Lo found in data from a sleep clinic at the University of Marburg in Germany. It turns out the healthy subjects' waking periods exhibited what's called a power-law distribution, which means that there is a direct correlation between the degree of awakeness and how often it occurs. A follow-up study showed that waking periods of people with sleep apnea, a breathing disorder that greatly disturbs sleep, also exhibit a power-law distribution, although at a different level. The same applied for subjects of different ages, surprising again because sleep patterns change as we get older. "This means that you have something very deeply fundamental to the process of sleep regulation," says research associate Plamen Ivanov.

Odder still, Lo and his colleagues say, is that the periods of sleep follow an entirely different pattern, called exponential distribution. That is, instead of an exact relationship between the length of time sleeping and how often waking occurs, the characteristic time scale changes during the night.

In all their research the physicists had never come across a natural system that exhibited both types of distributions, and they are at a loss to explain it. But another dual-distribution system recently turned up in the literature: avalanching sandpiles. Think of an hourglass: sand passes through the funnel, creating a pile below. Soon that pile collapses in an avalanche, and another starts building up. It too avalanches, and the pattern continues until the sand runs out. The avalanches follow a power-law distribution, just as the wake periods do during normal sleep, but the distribution of the quiet periods between avalanches follows an exponential distribution, as does sleep.

So what's going on here, and why should we care? For starters, sleep-inducing drugs could be better analyzed to check their efficacy, says Ivanov, by checking patients' sleep patterns, seeing if there is any change in the statistics of awakenings.

But there's another reason. Some scientists are beginning to think that all these phenomena — the similar power-law patterns in many natural systems, from earthquakes to sleep — "are manifestations of something very deep underneath," says Physics Professor H. Eugene Stanley, director of the Center for Polymer Studies. Before Newton, for example, the motion of an object dropped straight down and another tossed in a parabola didn't seem related. But with Newton's law of universal gravitation — the consequence of that apocryphal apple falling on his head — it was realized that both are described by a single law. "People think there is something lurking here — we don't understand it," says Stanley. It's enough to keep some folks up nights thinking about sleep and sandpiles. — *Taylor McNeil*

Brain Power

Researchers Study the Role of Choline in Brain Development and Aging

THE NUTRIENT CHOLINE is essential to human life. It's an integral component of all cell membranes in the body and an important part of a healthy diet. Lack of choline can lead to liver damage in adults. Choline is found in meats, vegetables, and other foods. And here's something else to think about the next time you're at the supermarket: choline may improve memory and learning.

A team of scientists, including Jan Krzysztof Blusztajn, a professor of pathology and laboratory medicine at the School of Medicine, is studying the effects of choline on brain development and aging in rats. Their research shows that rats that received choline at two key stages of development — in the second half of their twenty-two-day gestation period and from two to four weeks after birth — performed better on learning and memory tests than animals that didn't get any supplemental choline. And a little bit seems to go a long way: the scientists determined that as the rats grew older, those that received extra choline showed no age-related declines in memory.

Blusztajn says choline alters some cell functions in the brain, such as cell division. "You could say that the brain seems to be making more cells with choline supplementation," he explains. But what accounts for the long-lasting improvement in memory in the rats that receive extra choline before and after birth? It turns out that these rats experience changes in the hippocampus, a region of the brain important in learning and memory. Blusztajn and colleagues from the School of Medicine, Duke University, and the University of North Carolina at Chapel Hill are using a variety of methods to find out exactly what changes are taking place.

Blusztajn says that these rats may have a larger memory capacity than the rats that didn't receive extra choline. "And even when they are old and we test their performance, we don't detect declines," he says. "Maybe they are already deteriorating, and we're just giving them too easy a test. But the test is too difficult for the control animals, so somehow this prenatal supplementation generates a brain that is more resistant to those age-induced memory declines."

Scientists don't know yet if choline has similar effects on the human brain. In 1998 the National Academy of Science's Institute of Food and Medicine issued recommendations about how much choline people at various stages of life should consume to maintain overall good health. The nutrient is found in most foods, but is especially

Published online 24 March 2003 | Nature | doi:10.1038/news030317-13

News

Prime numbers not so random?

A kind of order may be buried in the occurrence of indivisible numbers.

Philip Ball

A team of physicists may have stumbled upon a surprising discovery about one of the deepest and best-studied questions in pure mathematics: whether or not prime numbers appear randomly in the sequence of whole numbers.

Primes cannot be divided by any smaller whole number other than 1.

Pradeep Kumar and colleagues at Boston University[1] reckon that they have found a kind of order among the distribution of primes, the numbers that cannot be divided by any smaller number other than 1.

The first few primes are 2, 3, 5, 7, 11 and 13; the largest currently known has over 4 million digits. No one has yet proved that their occurrence follows any pattern, or whether there is definitely no pattern.

Kumar's team looked at the increments in the intervals between consecutive primes. For example, the intervals between the first few are 1, 2, 2, 4 and 2. The increments are the differences between these successive intervals: +1, 0, +2 and -2.

These increments are not random, the physicists conclude: they have a rough-and-ready predictability. "Positive values are almost every time followed by corresponding negative values," explains team member Plamen Ivanov. That is clearly already true for the third and fourth increments above: +2 and -2.

The researchers are not experts in number theory, the relevant branch of pure mathematics. In fact, they did not set out to study the statistics of prime numbers at all. Ivanov suggested that his graduate student Kumar use primes merely to dry-run a statistical tool that they had developed to study heartbeat rhythms.

While probing the variations of the gaps between heartbeats, the researchers found something else. A plot of the number of increments of different sizes shows oscillations with a period of three.

That is to say, increments of plus or minus 6, 12, 18, and so on, are statistically less likely than increments of other sizes. Excepting the first in the series, the increments are even numbers, as all primes other than 2 are odd. That's why this oscillation has a period of 3 rather than 6, as it appears to have.

This finding is less surprising. Previous studies found period-6 oscillations in the histogram of distances between consecutive primes. Increments, remember, are differences between consecutive distances.

The Boston team's findings are not supported by any kind of rigorous mathematical proof. So sadly they can't shed any light on one of the biggest problems in maths: the Riemann hypothesis. This conjecture in number theory is intimately related to the distribution of primes. In 2001 the Clay Institute in the USA offered a prize of a million dollars for a proof of the Riemann hypothesis.

But The findings might have implications in the real world, as some systems in physics and biology - such as interacting prey and predator species with different life cycles - show patterns that depend on prime numbers.

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1. Kumar, P. Ivanov, P. C. Stanley, H. E. Information entropy and correlations in prime numbers. Preprint. http://xxx.lanl.gov/abs/cond-mat/0303110 (2003).

Nature ISSN 1744-7933 EISSN 1476-4687

PHYSICS NEWS UPDATE -- Number 713 December 27, 2004 by Ph Schewe, Ben Stein

From: Sam Wormley (*swormley1_at_mchsi.com*)
Date: 12/27/04

- **Next message:** Sergey Karavashkin: "For Y.Porat from Sergey Karavashkin on Quantum Paradox"
- **Previous message:** Last Timer: "Re: Quarks"
- **Messages sorted by:** [date] [thread]

Date: Mon, 27 Dec 2004 23:12:48 GMT

PHYSICS NEWS UPDATE
The American Institute of Physics Bulletin of Physics News
Number 713 December 27, 2004 by Phillip F. Schewe, Ben Stein

WHY DO HEART ATTACKS OCCUR MOST FREQUENTLY BETWEEN 9 AND 11 AM? Studying five healthy volunteers for 10-day periods in pioneering efforts to ultimately answer this question, a collaboration of Boston University physicists and Harvard physiologists has found evidence that the body's circadian clock (a part of the brain that regulates daily biological activities) influences patterns in the heart's "interbeat intervals," the lengths of time between successive heartbeats. At around 10AM for all the healthy individuals, the values of successive interbeat intervals displayed increased signs of randomness, statistically resembling that seen in previous studies of individuals with heart disease. In their studies, the researchers took special care to isolate the effects of a person's internal circadian clock (which has a 24.2-hour rhythm, marked by a regular rise and fall of body temperature) from the effects of behavior (such as physical activity and a person's wake/sleep time) or external stimuli (such as the rising or setting of the sun). Towards these ends, the researchers made sure to "desynchronize" the individuals' internal body clocks from these other factors by keeping the volunteers in a dimly lit room and by varying their sleep and wake times from day to day while keeping activity levels relatively constant.
The researchers next plan to explore how an individual's behavior may interact with the circadian clock to influence the correlations in interbeat intervals. The researchers have not yet studied patients with heart disease and are far from being able to make clinical recommendations. However, their further research may obtain insights into the underlying causes of increased cardiac risk and could lead to improved therapy, such as more appropriately timed medication to coincide with phases of the body clock. (Hu et al., Proceedings of the National Academy of Sciences, December 28, 2004; contact Plamen Ch. Ivanov, Boston University, 617-353-3891, plamen@argento.bu.edu; Steven Shea, Harvard Medical School, 617-732-5013, sshea@hms.harvard.edu)

A PEA-SIZED MAGNETOMETER can do the job of much bigger units, and measure magnetic fields with a sensitivity of 50 pico-tesla. Researchers at NIST exploit the fact that rubidium atoms possess quantum levels whose energies will depend on the ambient magnetic field. By encapsulating a tiny portion of atoms in a cell and making precision measurements of laser light traveling through the atoms, a field reading can be made. All of this is packaged in only about 12 cubic millimeters. Furthermore, the device can be manufactured in large batches through lithographic means. For geophysical applications, such as for detecting underwater or underground iron objects such as pipelines, tanks, and shipwrecks, the device's tiny power consumption, compact size, and low price should move it ahead of several existing magnetometer designs with a few more years of development work. (Schwindt et al., Applied Physics Letters, 27 December 2004; contact Peter Schwindt, schwindt@boulder.nist.gov, 303-497-7969; lab website at www.boulder.nist.gov/timefreq/ofm/smallclock/CSAM.htm)

DNA STRETCHING CROSS-STREAM. A new experiment shows that in specially engineered fluid flows typical of coating processes, single DNA molecules can sometimes enter into a kind of flow instability in which the DNA orients itself perpendicular to the plane of the flow. The
experiment, conducted at Rice University by Matteo Pasquali and Rajat Duggal, was part of a broader study of how polymer molecules behave in moving fluids, a subject pertinent to many biological and technological research areas, such as inkjet printing, paper coating, the movement of air in lung alveoli, and DNA arrays. Studying polymers in complex fluid flows is difficult because single polymers are hard to resolve (being typically only 10-100 nm in size) and because polymers can influence each other and the flow itself even at very low concentration (down to few parts per million). That's why DNA (above 10 microns in contour length) was chosen and why the DNA was kept "ultradilute," so that it would not influence the flow and that only DNA molecule is visible at a time. In the Rice experiment, a dilute suspension of DNA in water thickened by sugar is taken up by a rotating drum which moves past a glass knife edge. In this way a thin slice of solution can be moved as if on a conveyor belt past a lens. The lens focuses a blue-green light on the DNA and picks up green-yellow light emitted by the previously fluorescently-stained DNA molecules. The resulting 30-frame-per-second film clearly can image
individual DNAs at a time with a spatial resolution of 250 nm (the thickness of the molecule cannot be resolved but its length can be). The researchers had expected that in the complex flow (a flow in which the velocity of the fluid varies across the width of the channel) the DNA
would deploy itself with the flow rather than at right angles. Indeed, this happened at the lowest drum rotation speeds; the direction of stretching changed once the drum speed became high enough to induce ripples on the surface of the liquid moving past the glass knife. (Journal of Rheology, July/August 2004)

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- **Next message:** Sergey Karavashkin: "For Y.Porat from Sergey Karavashkin on Quantum Paradox"
- **Previous message:** Last Timer: "Re: Quarks"
- **Messages sorted by:** [date] [thread]

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  (sci.physics)
- Re: ID and the Difference Between Spheres and Cubes
  ... of **DNA** and the ability of cells to repair DNA. **...** There's nothing "ideological" about the observation that **mutations ...** What the hell is the **"quantum state"** of DNA? **...** Richard Feyman said, nobody understands **quantum physics). ...**
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- Re: The Origin of Life as Interpreted by Model Mechanics
  ... Current **physics** doesn't explain the trouble in Iraq, **...** The **CRE force** is a natural part of my theory. **...** Then why don't **DNA molecules** of the same size split apart **...** attractive EM force that forms the **DNA strand** the strand will split in half **...**
  (talk.origins)
- Re: The Origin of Life as Interpreted by Model Mechanics
  ... Sub-atomic physics must play a significant role simply because all matter on **...** When the **DNA molecule** grows in size the **... CRE force** also grows proportionately. **...** attractive EM force that forms the **DNA strand** the strand will split in half **...**
  (talk.origins)
- Re: Preventing Hoax Belief
  ... the **Moon** for the U.S.?") out of 22 there's but the top two messages **...** You'd think that a mere one or two counts of **gamma** per cm2 per second **... DNA** it supposedly isn't all that insurmountable as long as sufficient **...** as such seems to beg for some **honest physics math. ...**
  (sci.space.history)

Inside Science Research — Physics News Update

Number 679 #2, April 1, 2004 by Phil Schewe and Ben Stein

Migraine Sufferers Exhibit "Hypersynchronized" Brain Activity

Migraine sufferers exhibit "hypersynchronized" brain activity compared to those without migraines, reported researchers at **last week's APS March Meeting (http://www.aps.org/meet/MAR04)** . Sebino Stramaglia of the University of Bari (Sebastiano.Stramaglia@ba.infn.it) and his colleagues in Italy and at Boston University in the US have found that the brains of people with migraines respond differently than those without migraines.

The researchers flashed a series of repeating visual patterns to 15 healthy subjects and 15 migraine sufferers. In each of these human subjects, the visual patterns stimulated electrical signals in different regions of the brain.

The brain responds with its own rhythms: as neurons fire simultaneously, the electrical responses add together. The resulting EEG signal is then broken down into various components, such as alpha rhythms (8-12.5 Hz) which are associated with quiet wakefulness with eyes closed.

In patients with migraines, different areas of the cerebral cortex synchronized their alpha-wave signals much more closely with one another than those in healthy patients.

Such synchronization patterns speak to the possibility of an over-active, "hyper-synchronized" regulatory mechanism in the brains of people who suffer from migraines. This finding might provide clues on what causes the severe headaches--and how to prevent them. (**Paper W9.001 (http://www.aps.org/meet/MAR04/baps/abs/S8090001.html)**)

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MEDIA RELATIONS

News Releases

For Release Upon Receipt - December 20, 2004
Contact: Ann Marie Menting, 617/353-2240, amenting@bu.edu

BODY'S BIOLOGICAL CLOCK FOUND TO AFFECT CARDIAC RHYTHM PATTERNS IN HEALTHY ADULTS

Statistical physics approach to analysis of heartbeat pattern uncovers link to circadian cycle

(Boston) — In a newly reported, first-ever finding, physicists from Boston University and physiologists from Boston's Brigham and Women's Hospital (BWH) have found that the body's biological clock affects the patterns of heart-rate control in healthy individuals independent of sleep/wake cycle or other behavior influences. Their analysis of the heartbeat dynamics of the healthy individuals in the study showed significant circadian rhythm, including a notable response at the internal circadian phase corresponding to 10 a.m., the time of day most often linked to adverse cardiac events in individuals with heart disease.

The BU/BWH team will report its findings in the Dec. 28 issue of the *Proceedings of the National Academy of Sciences*. Sponsored by grants from the National Institutes of Health, the institutional teams were led by Plamen Ivanov, a research associate in BU's Center for Polymer Studies, who undertook the analysis of the data, and Steven Shea, director of BWH's medical chronobiology program and associate professor of medicine at Harvard Medical School, who conducted the experimental part of the research.

Cardiac disease is the leading cause of death in the United States, accounting for 29 percent of the deaths from the nation's 10 leading causes (including homicides and accidents), according to the latest statistics (2001) available from the National Center for Health Statistics.

When designing their study of this deadly disease, the BU/BWH team drew on seemingly disparate findings in epidemiology, cardiology, circadian biology, biomedical engineering, and physics to construct an approach that would assess heartbeat fluctuations in healthy individuals at different circadian phases. In addition, they choose to analyze the data from these individuals using tools from statistical physics that describe relationships between the frequencies of large and small events. With these tools, the researchers hoped to find whether underlying patterns in the heartbeat data of the study participants were affected by the circadian phases.

For more than a decade, researchers at the Center for Polymer Studies have applied statistical physics methods to investigations of cardiac dynamics, probing for hidden patterns. Previous statistical evaluations of heartbeat fluctuations by Ivanov and others have shown that those of healthy subjects exhibit a self-similar structure over a range of time scales, that is, the fluctuations found in a window of 10 beats will be statistically similar to those found in a heartbeat interval of 100 beats and or one of 1000 beats.

"These studies have demonstrated that this self-similar structure in the temporal order of heartbeat fluctuations changes with certain behaviors, such as sleep or wake, rest or exercise," explains Ivanov. "Based on these observations, we hypothesized that these dynamic patterns will also change with circadian rhythm. This provided the impetus for the study design."

Epidemiological studies, too, have shown a pattern to events associated with heartbeat irregularities such

as myocardial infarction, stroke, angina, arrhythmias and sudden cardiac death. These events have been found to have a strong 24-hour day/night pattern and, intriguingly, have been found to occur most often around 10 a.m.
Day/night patterns of disease severity are often associated with sleep/wake behavior but, the researchers hypothesized, they can also be linked to an internal body clock, the endogenous circadian pacemaker that controls much of our physiology, even when behaviors are unchanged. Body temperature, Shea notes, rises during the day and falls at night even when a person doesn't sleep at night. The circadian cycle usually "resets" itself daily in response to certain external cues, most especially bright light, such as sunlight.

To remove any influence from the sleep/wake cycle, Shea and his team employed a "forced desynchrony" protocol on the five healthy volunteers who participated in the study. For 10 days, the participants lived in dimly lit rooms cut off from any outside stimuli or time cues. The researchers adjusted scheduled behaviors (sleeping periods, eating, and the like), gradually shifting the behavior patterns until the participants had a 28-hour day, about 19 hours awake and 9 hours asleep. This 28-hour sleep/wake schedule was sustained for seven "days," while core body temperatures, used to mark participants' internal circadian phases, continued to oscillate with an approximate 24-hour period, indicating their sleep/wake cycles had been experimentally separated from their circadian cycles.

Using heartbeat data gathered from the participants throughout the 10-day desynchrony, Ivanov and BU team members Kun Hu and Zhi Chen, research assistants in physics, estimated correlations in the heartbeat fluctuations according to a power law function quantified using a method known as a detrended fluctuation analysis (DFA). The DFA mathematically describes the fluctuations at different time scales in the heartbeat signal and produces a scaling exponent that characterizes the degree of correlation between heartbeat intervals. If, for example, the scaling exponent, known as α, equaled 0.5, the interval fluctuations showed no correlation; if α equaled 1.5, the interval fluctuations were considered to be without control, exhibiting a so-called random walk property. If, however, α fell between 0.5 and 1.5, the interval fluctuations were considered to be organized and physiologically controlled. Interestingly, research studies have associated α values progressing toward 1.5 with pathological conditions, such as congestive heart failure.

When the team analyzed wake period data, they found a striking correlation: α values changed according to the internal body clock time. At 2 a.m., the value was 0.8; at 5 p.m., it was 1.0. However, at 10 a.m., the time of day found to have the greatest incidence of cardiac incidents, the team found the value was 1.2, edging toward the value linked with congestive heart failure. The team likewise found strong circadian rhythms whether data were considered only from the awake period or only from the sleep period.

"We are tempted to speculate that if the same circadian effect occurs in people with diseased hearts, then this may contribute to the day/night pattern of cardiac events," says BWH's Shea. "But this was only a study on healthy subjects, and, therefore, we are a long way from making clinical recommendations. Further studies could, however, provide insight to the underlying cause of the disease — and to therapies that might work better by being timed to the specific phases of the body clock."

Brigham and Women's Hospital is a 735-bed nonprofit teaching affiliate of Harvard Medical School and a founding member of Partners HealthCare System, an integrated health care delivery network. Internationally recognized as a leading academic health care institution, BWH is committed to excellence in patient care, medical research, and the training and education of health care professionals.

Scientists at Boston University's Center for Polymer Studies, part of BU's Department of Physics in the College and Graduate School of Arts and Sciences, research polymer systems at the microscopic level, focusing on describing the basic spatial configurations of polymer molecules so as to better predict the macroscopic behavior of polymers. Interdisciplinary science research at the Center includes studies of cardiac dynamics, the statistical mechanisms of Alzheimer's disease, and simulations of liquid water. Boston University, with an enrollment of more than 29,000 in its 17 schools and colleges, is the fourth-

Inside Science Research — Physics News Update

Number 713 #1, December 27, 2004 by Phil Schewe and Ben Stein

Why Do Heart Attacks Occur Most Frequently Between 9 And 11 Am?

Studying five healthy volunteers for 10-day periods in pioneering efforts to ultimately answer this question, a collaboration of Boston University physicists and Harvard physiologists has found evidence that the body's circadian clock (a part of the brain that regulates daily biological activities) influences patterns in the heart's "interbeat intervals," the lengths of time between successive heartbeats. At around 10AM for all the healthy individuals, the values of successive interbeat intervals displayed increased signs of randomness, statistically resembling that seen in previous studies of individuals with heart disease.

In their studies, the researchers took special care to isolate the effects of a person's internal circadian clock (which has a 24.2-hour rhythm, marked by a regular rise and fall of body temperature) from the effects of behavior (such as physical activity and a person's wake/sleep time) or external stimuli (such as the rising or setting of the sun). Towards these ends, the researchers made sure to "desynchronize" the individuals' internal body clocks from these other factors by keeping the volunteers in a dimly lit room and by varying their sleep and wake times from day to day while keeping activity levels relatively constant.

The researchers next plan to explore how an individual's behavior may interact with the circadian clock to influence the correlations in interbeat intervals. The researchers have not yet studied patients with heart disease and are far from being able to make clinical recommendations. However, their further research may obtain insights into the underlying causes of increased cardiac risk and could lead to improved therapy, such as more appropriately timed medication to coincide with phases of the body clock. (Hu *et al.*, **Proceedings of the National Academy of Sciences (http://www.pnas.org/)** , December 28, 2004; contact Plamen Ch. Ivanov, Boston University, 617-353-3891, plamen@argento.bu.edu; Steven Shea, Harvard Medical School, 617-732-5013, sshea@hms.harvard.edu)

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Published online 7 January 2004 | Nature | doi:10.1038/news040105-4

News

Techno hits basic beat

Musical analysis unveils a hierarchy of sophistication.

Philip Ball

A form of music known as Javanese Gamelan has won one of the top prizes for rhythmic complexity, according to a novel kind of musical analysis[1].

Gamelan music is sophisticated but not as good for dancing as techno beats.

© *alamy.com*

Heather Jennings of the Federal University of Alagoas in Brazil and her colleagues conclude that Gamelan - an Indonesian style of music featuring gongs, drums, wind and string instruments - is as sophisticated as Western classical music in terms of its variations in volume. And both of these styles tower in complexity over modern techno tracks and Forró, a form of traditional dance music from Brazil.

Jazz, rock and roll and Brazilian pop music lie between the two extremes, the researchers say. They are "complex enough to listen to, but periodic and rhythmic enough to dance to", they write.

But music snobs shouldn't think that complex music is necessarily better than simpler varieties. Both techno and Forró have a strong, regular rhythm that is perfect for dancing, the paper points out.

Measuring the rhythmicity of music might seem a simple matter, but in fact it's surprisingly tricky.

Acoustic scientists studying complex sounds typically measure their 'power spectra': a measure of the patterns with which volume changes over time. For music with a thumping, regular rhythm, for example, the loudness power spectrum would have a peak corresponding to the main beat.

But power spectra are rather crude measures, Jennings and colleagues say, and can hide some of the complexities of different musical forms. For one thing, a power spectrum might not distinguish a series of sequential changes in rhythm from several overlapping rhythms.

To get around this, the researchers fed four-minute stretches of music into a more sophisticated technique, called detrended fluctuation analysis (DFA). This has been used in the past to study complicated signals in economic, genetic and heartbeat data.

The method produces a number, denoted alpha that quantifies the complexity of patterns in a signal - in this case, the volume of music. A low alpha (less than 1) indicates relatively non-complex music, whereas more complex musical signals have a value of alpha closer to 1. Music with alpha larger than 1 will tend to have long patches of loud and quiet, and will tend to be quite boring, says coworker Plamen Ivanov of Boston University in Massachusetts. But for alpha=1, the sound will probably be judged more interesting and pleasant, he says.

Gamelan has average values of alpha closest to 1, as does what the researchers characterize as 'new age music'. The averages for Western classical and Hindustani music are slightly higher.

Curiously, jazz and rock and roll have virtually identical average alpha values of about 0.9, challenging the notion that the latter is in some ways a debased, simplified version of the former. But then, in music, rhythm isn't everything.

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1. Jennings, H. D., Ivanov, P. Ch., Martins, A. M., da Silva, P. C. & Viswanathan, G. M. Variance fluctuations in nonstationary time series: a comparative study of music genres. *Preprint*, http://xxx.lanl.gov/abs/cond-mat/0312380 (2003).

Nature ISSN 1744-7933 EISSN 1476-4687

Physics 108 - Physics News Items

I will post here various items (when I notice them) of physics in the news, in particular, applications of physics to the life sciences that you might be interested in, and that have relevance to our class.

- **NANOPORES AND ZEPTOMOLE BIOLOGY**. Some proteins naturally form nanometer-scale pores that serve as channels for useful biochemical ions. Through this ionic communication, nanopores enable many functions in cells, such as allowing nerve cells to communicate (they are even responsible for twitching the frog leg in Galvani's famous discovery in the 1700s). Nanopores can be destructive too. When the proteins of bacteria and viruses attach to a cell, their nanopores can facilitate infection, for example by shooting viral DNA through them into the cell. At the APS (American Physical Society) March Meeting, NIST's John J. Kasianowicz (john.kasianowicz@nist.gov) showed how single biological nanopores can be used to detect and characterize individual molecules of RNA and DNA. He also demonstrated constructive uses for anthrax-related nanopores in diagnosing anthrax infections and testing anti-anthrax drugs. Anthrax bacteria secrete a protein called "protective antigen" that attaches to an organic membrane such as a cell wall. The protein forms a nanopore that penetrates the membrane. When another anthrax protein called "lethal factor" attaches to the protective antigen nanopore, it prevents ionic current from flowing through the pore (and out of the organic membrane). By monitoring animal blood samples for changes in ion current, Kasianowicz and his colleagues at the National Cancer Institute and the United States Army Medical Research Institute for Infectious Diseases electronically detected a complex of two anthrax proteins in less than an hour, as opposed to the existing methods which can take up to several days. Also, they demonstrated a method for screening potential therapeutic agents against anthrax toxins using the anthrax nanopore (see http://www.nist.gov/public_affairs/techbeat/tb2005_0826.htm#anthrax for a picture and more information).

  A Brown University group led by Sean Ling (Xinsheng_Ling@brown.edu) was among those reporting progress in developing a nanopore-based method for sequencing DNA faster and more cheaply than traditional biochemical techniques. In one scenario the change in ion current as DNA moves through the nanopore could yield the sequence of bases (letters) in the DNA. However, the letters in DNA are so close to each other (about 4 angstroms) and the DNA moves so quickly through the nanopore that researchers have had to come up with creative solutions for reading the individual letters. For example, the Brown group attaches complementary blocks of DNA, about 6 letters long, to the DNA sequence of interest, so that the researchers would read blocks of multiple letters at a time, while slowing down the passage of the DNA by attaching a magnetic bead to it. Other researchers are finding value in developing nanopores for fundamental biology studies. Discussing his group's latest work with artificial, silicon-based nanopores, Cees Dekker of the Delft University of Technology (dekker@mb.tn.tudelft.nl) showed how lasers and other manipulations with the artificial pores are enabling new single-molecule (zeptomolar) biophysics studies on the properties of DNA, RNA, and proteins by studying how they pass through the pores (see www.aip.org/png for an artist's rendering of DNA traversing through a nanopore)

  From: The American Institute of Physics Bulletin of Physics News Number 770 March 23, 2006 by Phillip F. Schewe, Ben Stein

- **BREAST CANCER DETECTION AND NUCLEAR PHYSICS** at Jefferson Lab.
  More information available here; A William & Mary graduate student, Daniella Steinbach, worked on part of this for her dissertation.

- **OUR SIXTH SENSE IS AS FINE TUNED AS IT CAN BE** says Todd Squires, a physicist at Caltech. He has investigated why the natural selection process, operating over evolutionary time, settled upon specific dimensions for the vestibular semicircular canals (SCC), the set of three mutually perpendicular, fluid-filled tubes housed in the inner ear of vertebrates that give an organism its sense of balance. Scientists sometimes recognize the perception of balance and motion as being a sixth sense, in addition to the usual five---smell, touch, sight, hearing, and taste. The balance sense organ, the SCC structures, are essentially donut-shaped, with a major radius of 3 mm and minor radius of 0.2 mm. Furthermore, the torus is interrupted by a membrane called a cupula impregnated with tiny sensory hairs for sensing the sloshing of the fluid through the canals. Sensing an acceleration or rotation involves the fluid being momentarily left behind while the head (and the SCCs) rotate in a new direction. The fluid displaces the cupula, deflecting the sensory hairs and triggering a neural signal to the brain and muscles controlling the eye, and this is what gives us the sense of motion, and sometimes dizziness. Squires addressed himself to the question of why the SCC should be roughly the same size (to within a factor of three) in mice as it is in whales. In humans, for instance, the SCC reaches its full adult size in about the 14th week of pregnancy. Why should SCCs be all of this one size, as if evolutionary pressures had "converged" on an optimal solution? In performing studies of optimal design, Squires varied four different key physical parameters---SCC major radius, minor radius, cupula thickness and height---and discovered that the greatest canal sensitivity occurred for those parameter values manifested in actual vertebrates. Knowing how the canals work is important for understanding various forms of dizziness (such as "top-shelf vertigo," the light-headedness experienced by some when they tilt their heads back in looking at a top shelf) and for understanding peculiarities of some ordinary visual experiences. For example, since the SCC output is wired into eye-control muscles, some motions can be compensated: you can read a fixed page while swiveling your head, but with your head fixed you can't read a page swivelled by a friend. The SCC-eye feedback effect also explains why some home video, recorded while the filmer is in motion, doesn't look so good afterwards in the editing stage, when the neuro-feedback mechanism isn't at work. (Todd Squires, Physical Review Letters, 5 Nov 2004; tsquires@acm.caltech.edu, 626-395-4640; for further background, see Scientific American, 243, p118, 1980)

  From: The American Institute of Physics Bulletin of Physics News Number 741 August 12, 2005 by Phillip F. Schewe, Ben Stein

- **NUCLEAR IMAGING OF IODINE UPTAKE IN MICE**; a joint Jefferson Lab and W & M project

- **A NEW "PHASE" FOR BIOLOGICAL IMAGING**. Researchers have demonstrated a practical x-ray device that provides 2- and 3-dimensional images of soft biological tissue with details that are ordinarily hard to discern with conventional x-ray imaging. Performed by researchers at the Paul Scherrer Institut in Switzerland and the European Synchrotron Radiation Facility in France (Timm Weitkamp, timm.weitkamp@psi.ch), this work may help facilitate advanced medical applications of x rays, such as the ability to detect cancerous breast tissue directly, rather than the hard-tissue calcifications that are produced in later stages of the disease. X rays excel at imaging hard tissue--such as teeth--as well as the contrast between hard and soft tissue--such as bones and skin in the human hand. However, x-rays are ordinarily not good at distinguishing between different types of soft tissue, such as normal and cancerous breast cells. Optics researchers have long shown that x-rays have the potential to image different kinds of soft tissue through a technique known as "phase" imaging. When an x ray encounters the boundary of two types of material, such as normal tissue and cancerous tissue, it will undergo a "phase shift": the peak of the wave will move backward by a small amount relative to the position where it would be if there were no sample in the beam. By measuring the phase shifts as x rays pass from one type of soft tissue to another, researchers can distinguish between the two, and can produce a practical image unattainable before. While phase-based imaging devices have been previously constructed, none has yet been widely adopted for medical diagnosis. The new device has three attributes needed for widespread medical use--compact size (only a few centimeters in length), large field of view (up to 20x20 cm^2), and the ability to use polychromatic x-rays rather than more difficult-to-obtain monochromatic sources. The main innovation in the new design is that it uses a pair of gratings--each a thin slab of material with narrow, closely spaced parallel lines etched deeply into them, like little slits carved into the inch marks of a ruler. As they pass through the object to be imaged, the x rays undergo a series of phase shifts. Passing next through the first grating, the x rays stream is diffracted into multiple waves that combine and interfere to produce a series of fringes (bright and dark stripes). The second grating extracts from this pattern precise information on the inner details of the object. Using this technique, the researchers imaged a small spider, revealing internal structures that would be difficult to image with any other method. The researchers believe that the modest requirements of this technique, in terms of the x-ray source, laboratory space, and materials, may make phase-based imaging practical for a wide range of biological and medical applications. (Weitkamp et al., Optics Express, August 8, 2005, text available at http://www.opticsexpress.org /abstract.cfm?URI=OPEX-13-16-6296; For background information, see "Phase Sensitive X-ray Imaging" in Physics Today, July 2000; graphics and more details at osa.org/news/release/08.2005/contrast_imager_newphasemed.asp)

From: The American Institute of Physics Bulletin of Physics News Number 741 August 12, 2005 by Phillip F. Schewe, Ben Stein

- **A NANOSCALE GALVANI EXPERIMENT** provides a new way to obtain images of biological tissue. Applying state-of-the-art technology to a seldom-exploited electromechanical property in biomolecules, Sergei Kalinin of Oak Ridge National Laboratory (sv9@ornl.gov) and his colleagues have demonstrated a nanometer-scale version of Galvani's experiment, in which 18th-century Italian physician Luigi Galvani caused a frog's muscle to contract when he touched it with an electrically charged metal scalpel. Described at this week's AVS Science & Technology meeting in Boston, the new, 21st-century demonstration promises to yield a host of previously unknown information in a variety of biological structures including cartilage, teeth, and even butterfly wings. Employing a technique named Piezoresponse Force Microscopy (PFM), Kalinin and colleagues sent an electrical voltage through a tiny, nanometer-sized tip to induce mechanical motion along various points in a biological sample, such as a single fibril of the protein collagen. The electromechanical response at various points of the sample, as measured by the probe tip, enabled the researchers to build up images of the collagen fibrils, with details less than 10 nanometers in size. This resolution surpasses the level of detail that can be gleaned on those biostructures by ordinary scanning-probe and electron microscopes (get a lengthier description at http://www2.avs.org/symposium/boston/pressroom/papers.html). The PFM technique exploits the well-known but infrequently used fact that many biomolecules, especially those that are made of groups of proteins, are piezoelectric, or undergo mechanical deformations in the presence of an external electric field. The researchers have used the PFM technique to produce images of cartilage as well as enamel and dentin (found inside teeth). Besides providing images of biostructures on a nanometer scale, the new technique yields vinformation about the electromechanical properties and molecular orientation of biological tissue. In recent work, the researchers even found unexpected piezoelectric properties in butterfly wings which enabled them to yield molecular-level images of wing structures. (Kalinin, Rodriguez and Gruverman, meeting paper NS-WeM3)

  From: The American Institute of Physics Bulletin of Physics News Number 752 November 2, 2005 by Phillip F. Schewe, Ben Stein

- **LASER SCATTERING OF MITOCHONDRIA** the "power plants" of cells, can immediately identify early-stage liver cancer cells and potentially monitor stem cells as they undergo various stages of development. At the APS March Meeting, Paul Gourley of Sandia (plgourl@sandia.gov) reported the latest uses of the "biocavity laser," an aluminum-gallium-arsenide based design that continuously pumps in single human cells into a chamber for analysis. The laser's beams are altered in their passage through the cells. The 800-nanometer light in the experiments is not absorbed by most of the cell, except by its hundreds of mitochondria, which are responsible for scattering 90-95 percent of the light. By analyzing the scattering patterns, the researchers determined the distribution of mitochondria in the cell, and could instantly determine whether the cell was healthy (in which case the mitochondria cluster cooperatively around the cell nucleus) or cancerous (in which case they are apathetically sprawled across the cell). The process is highly accurate, works much more quickly than traditional techniques, and does not require the usual pre-treatment of cells with chemical reagents or fluorescent molecules. Co-author Bob Naviaux of UC-San Diego added the biocavity laser technique also has the potential to rapidly identify the in-between states of stem cells as they transform into their final identities.

  From: The American Institute of Physics Bulletin of Physics News Number 725, April 1 2005, by Phillip F. Schewe, Ben Stein

- **ZEPTOGRAM MASS DETECTION---WEIGHING MOLECULES.** Michael Roukes and his Caltech colleagues produce some of the finest nanoscopic electromechanical systems (NEMS) devices in the world. His latest achievement is performing mass measurements with nearly zeptogram (zg) sensitivity, that is, with an uncertainty of only a few times 10^-21 grams. At this level you can start to weigh molecules one at a time. In experiments, the presence of xenon accretions of only about 30 atoms (7 zg, or about 4 kilodaltons, or the same as for a small protein) have been detected in real time. Minuscule masses are measured through their effect on an oscillating doubly clamped silicon carbide beam, which serves as the frequency-determining element in a tuned circuit. So, in practice, the beam would be set to vibrating at a rate of more than 100 MHz and then would be exposed to a faint puff of biomolecules. Each molecule would strike the beam, where its presence (and its mass) would show up as a changed resonant frequency. After a short sampling time, the molecule would be removed and another brought in. Through this kind of miniaturization and automation, the NEMS approach to mass spectroscopy could change the way bioengineering approaches its task, especially in the search for cancer and its causes. The Roukes (roukes@caltech.edu, 626-395-2916) group reported its findings at last week's meeting of the American Physical Society (APS) in Los Angeles.

  From: The American Institute of Physics Bulletin of Physics News Number 725, April 1 2005, by Phillip F. Schewe, Ben Stein

- **HOW EFFECTIVE WILL FLU VACCINE BE?**A new way to study this important issue is to use the tools of statistical physics. At the APS meeting, Michael Deem of Rice University (mwdeem@rice.edu) described a new way of predicting the flu vaccine's efficacy (a higher efficacy means that fewer vaccinated individuals get the flu relative to unvaccinated individuals). To measure efficacy, researchers examine each strain's hemagglutinin (H) protein, the major protein on the surface of influenza A virus that is recognized by the immune system. In one standard approach, researchers study all the mutations in the entire H protein from one season to the next. In another approach, researchers study the ability of antibodies produced in ferrets to recognize either the vaccine strain or the mutated flu strain, which had been thought to be a good method for predicting flu vaccine efficacy in humans. However, these approaches are only modestly reliable indications of the vaccine's efficacy. Deem and his Rice University colleagues point out that each H protein has 5 "epitopes," antibody-triggering regions mutating at different rates. The Rice team refers to the one that mutates the most as the "dominant" epitope. Drawing upon theoretical tools originally developed for nuclear and condensed-matter physics, the researchers focus on the fraction of amino acids that change in the dominant epitope from one flu season to the next. Analyzing 35 years of epidemiological efficacy data, the researchers believe that their focus on epitope mutations correlates better with vaccine efficacy than do the traditional approaches. Deem and his colleagues Vishal Gupta and Robert Earl believe that this new measure may prove useful in designing the annual flu vaccine and in interpreting vaccine efficacy studies.

  From: The American Institute of Physics Bulletin of Physics News Number 724, March 25 2005, by Phillip F. Schewe, Ben Stein

- **PROTON BEAMS FOR CANCER THERAPY** Hampton University project

- **MEMORY AND CRITICAL AVALANCHES IN THE BRAIN.** Physicists at Indiana University are extending their study of the relation between observed patterns of neuron activity and memory storage in the brain. First came experimental work with slices of rat brain. Later the researchers performed simulations to try to emulate the data. Activity in the actual samples displayed two fascinating features: (1) the ensemble of neurons firing varies in size very much like "avalanche" phenomena such as occur in sandpiles and forest fires; and (2) there are stable activity patterns that resemble memory sequences measured in lab studies of rats in a maze. Every time a rat runs a particular route the same sequence of neural firings occur. At night the same sequence might be replayed as a rat "dream." If the rat's dream is interrupted, his ability to run the same route the next day might be compromised. This has added evidence to the notion that sleeping and dreaming help to consolidate memories from the previous day's activities. Stable activity patterns also appear in artificial neural networks as a way of storing information. The Indiana physicists take a fundamental look at those patterns. They used a 60-electrode array to look at firings in a thin slice of rat brain tissue. The cells in the slice, supplied with oxygen and nutrients, go on behaving as if they were part of a living brain. The general ensemble firing of cells is classified as subcritical (one cell firing leads, on the average, to less one additional cell firing), critical (one firing leads to another firing), or supercritical (a firing leads to two or more cells firing). In this regard, neural cells triggering each other are somewhat like chain reactions among uranium-235 atoms in a nuclear reactor. The subcritical case is uninteresting. The supercritical situation often leads to the case in which all the cells in the sample end up firing, which is also uninteresting. The critical case has the most to offer: neural ensembles of all sizes ensue. If you plot (with logarithmic rulings) the number of firing events versus the size of the firing ensemble, you get a straight line, indicative of classic "power law spectrum" behavior. In other words, the likelihood of an event (earthquake, sand avalanche, hurricane) of size E drops off according to E raised to a negative exponent. Now, in the simulation work, the notion that the most interesting outcomes occur when the brain system is maintained right at criticality is reinforced. The simulations, which do roughly match the observed behavior, are surprising and even counterintuitive. This is because precisely amid conditions which favor the greatest number of avalanches the largest number of stable neural activity patterns also occurs. One of the researchers, John M. Beggs, says that the work is meant to explore how avalanches in brain cells might be used to store information. (Haldeman and Beggs, Physical Review Letters, 11 February 2005,jmbeggs@indiana.edu, 812-855-7359; lab website, http://biocomplexity.indiana.edu/research/info/beggs.php)

From: The American Institute of Physics Bulletin of Physics News Number 719 February 10, 2005 by Phillip F. Schewe, Ben Stein

- **CONTROLLING BRAIN WAVES**. A new study conducted at George Mason University confirms predictions that electrical fields can be used to modify waves traveling through brain tissue. This is perhaps the first example of electric modification of neuronal thresholds to control wave movement. Indeed, it is one of the first times waves have been controlled in an excitable medium through changing thresholds. The researchers begin with a section of rat brain; the tissue consists of 6 layers of 2-dimensional sheets of neurons. A neural wave is initiated at one end of the network and the signal is observed at the other end. By using electrical fields, the excitability of individual neurons can be modified. Doing this can slow down, speed up, or stop any wave propagating through the sample. Previously neural waves had only been modified by pharmacological means. This action can be negated only by washing out the drug used, which takes seconds, whereas the electric method takes only microseconds to have an effect. One potential application for modifying brain waves would be in mitigating epileptic seizures. (Richardson et al., Physical Review Letters, 21 January 2005; lab website, www.neuraldynamics.org; contact Bruce Gluckman, bgluckma@gmu.edu, 703-993-4384 or Steven Schiff, sschiff@gmu.edu) Part of the George Mason contingent also was involved in the recent discovery of true spiral waves in the sensory cortex of the brain (Huang et al J Neurosci 24: 9897-9902, 2004).

  From: The American Institute of Physics Bulletin of Physics News Number 718 February 2, 2005 by Phillip F. Schewe, Ben Stein

- **A NEW APPROACH FOR CALMING PARKINSON'S TREMORS**. Many neuroscientists believe that pathological brain rhythms, for example in Parkinson's disease and in epilepsy, arise from an abnormal synchronization of many thousands of nerve cells (neurons). This physical mechanism appears in many physical and biological systems. For example, it enables fireflies to light up in unison. Sometimes, synchrony is desirable, for instance, when the cells of the heart's main pacemaker (the sino-atrial node) fire all together to stimulate heart contraction. But in many cases synchrony is harmful. London's Millennium Bridge, which swayed undesirably shortly after it opened in 2000, provides a useful example. Hundreds of pedestrians subconsciously synchronized their pace to the bridge's sideways, left-to-right swaying motions. The bridge oscillations, driven by pedestrians, became dangerously large, and the walkway had to be closed for reconstruction. In the case of a Parkinson's tremor one also needs to suppress the synchronous oscillations of nerve cells, but one can hardly apply the methods used by engineers for the Millennium Bridge. Thus, researchers need a technique to control the collective synchrony of neurons. Now, a paper suggests a new approach: one would measure the collective rhythm of nerve cells and, after some delay, electrically "feed back" this rhythm into the population of nerve cells. Adjusting the delay time and the amplification in the feedback loop, the researchers in principle could either suppress or enhance the collective rhythm. The researchers (Michael Rosenblum, mros@agnld.uni-potsdam.de, and Arkady Pikovsky, pikovsky@stat.physik.uni-potsdam.de, University of Potsdam, Germany) have tested this idea in simulations that employ mathematical models of neuron populations. The researchers believe the scheme might be used, in particular, for suppressing Parkinson's tremors by means of the emerging medical technique, called Deep Brain Stimulation, that enables intervention with the use of implanted microelectrodes. In principle, medical doctors could use an implanted electrode to measure electrical activity of the brain area and stimulate the nerve-cell population via a second electrode with the delayed signal. The advantage of this approach is that individual neurons are not much affected and continue to function, while the pathological collective Parkinsonian rhythm is suppressed noninvasively. (Rosenblum and Pikovsky, Physical Review Letters, upcoming article.)

  From: The American Institute of Physics Bulletin of Physics News Number 673 February 18, 2004 by Phillip F. Schewe, Ben Stein, and James Riordon

- **WHY DO HEART ATTACKS OCCUR MOST FREQUENTLY BETWEEN 9 AND 11 AM?** Studying five healthy volunteers for 10-day periods in pioneering efforts to ultimately answer this question, a collaboration of Boston University physicists and Harvard physiologists has found evidence that the body's circadian clock (a part of the brain that regulates daily biological activities) influences patterns in the heart's "interbeat intervals," the lengths of time between successive heartbeats. At around 10AM for all the healthy individuals, the values of successive interbeat intervals displayed increased signs of randomness, statistically resembling that seen in previous studies of individuals with heart disease. In their studies, the researchers took special care to isolate the effects of a person's internal circadian clock (which has a 24.2-hour rhythm, marked by a regular rise and fall of body temperature) from the effects of behavior (such as physical activity and a person's wake/sleep time) or external stimuli (such as the rising or setting of the sun). Towards these ends, the researchers made sure to "desynchronize" the individuals' internal body clocks from these other factors by keeping the volunteers in a dimly lit room and by varying their sleep and wake times from day to day while keeping activity levels relatively constant. The researchers next plan to explore how an individual's behavior may interact with the circadian clock to influence the correlations in interbeat intervals. The researchers have not yet studied patients with heart disease and are far from being able to make clinical recommendations. However, their further research may obtain insights into the underlying causes of increased cardiac risk and could lead to improved therapy, such as more appropriately timed medication to coincide with phases of the body clock. (Hu et al., Proceedings of the National Academy of Sciences, December 28, 2004; contact Plamen Ch. Ivanov, Boston University, 617-353-3891, plamen@argento.bu.edu; Steven Shea, Harvard Medical School, 617-732-5013, sshea@hms.harvard.edu)

  From: The American Institute of Physics Bulletin of Physics News Number 713 December 27, 2004 by Phillip F. Schewe, Ben Stein

- **FINDING A VEIN**, necessary for administering intravenous solutions, can often be difficult. A new device, called a Vein Contrast Enhancer (VCE), uses sensitive infrared sensing to find the vein beneath the skin and then also projects the rather spooky vein image back onto the patient's wrist. This makes it appear as if the veins were lying right on top, making it easy for a nurse to make an injection. How does it work? An array of light emitting diodes shines infrared light at the subject, and one depends on the fact that red blood cells scatter light differently from surrounding fatty tissue. The scattered light passes through some filters and then is captured by a CCD TV camera, processed by computer, and rendered as a sort of movie at a rate of 30 frames per second. These images can be projected onto the subject through a careful aligning process to register the surface projection with subcutaneous anatomy (see figure at www.aip.org/png). Herbert Zeman and his colleagues at the University of Tennessee Health Science Center in Memphis have done extensive clinical trials with VCE devices and are now doing trials with the projection capability. The general spatial resolution of the process is about 0.1 mm. Veins as deep as 8 mm have been imaged. This work is being presented at this week's Frontiers in Optics meeting in Rochester, co-sponsored by the Optical Society of America (OSA) and the American Physical Society (APS). (http://www.osa.org/meetings/annual/. See also http://www.conenhill.com/)

From: The American Institute of Physics Bulletin of Physics News Number 704 October 13, 2004 by Phillip F. Schewe, Ben Stein

last updated: March 23

[Physics 108: Physics for the Life Sciences](http://physics.wm.edu/~armd/P108_other_texts.html)
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NEWS AND VIEWS

Nature Medicine **11**, 125 (2005)
doi:10.1038/nm0205-125

Research Highlights

Rediscovering penicillin

β-lactam antibiotics such as penicillin protect neurons from death by upregulating expression of the glutamate transporter GLT1, report Jeffrey Rothstein *et al*. in the 6 January *Nature* (**433**, 73–77; 2005).

GLT1 mediates activity at the neuronal synapse, and in experimental models upregulation of the molecule can stave off neuronal damage. Such findings have prompted the fierce pursuit for a molecule that can positively modulate GLT1. To find such a molecule, the researchers screened a library of 1,040 FDA-approved compounds for their ability to increase GLT1 expression in cultured slices of spinal cord. A single class of compounds, the β-lactam antibiotics, came to the top.

β-lactam antibiotics kill bacteria by inhibiting synthesis of the cell wall. In neurons, the researchers found that the drugs upregulated the transcription of the gene encoding GLT1, through an as yet unexamined pathway. Both in culture and in mice, the drugs boosted expression of GLT1 threefold. In a model of spinal cord injury, treatment with penicillin and ceftriaxone prevented motor neuron loss. What's more, ceftriaxone could slow progression of symptoms in a mouse model of amyotrophic lateral sclerosis (ALS) which involves altered expression of glutamate transporters. The drug delayed loss of muscle strength and body weight in the mice and had a modest effect on prolonging lifespan.

Moving out

Strategies that promote movement of stem cells from the marrow to the bloodstream are used during hematopoietic stem cell transplantation. A key player in this mobilization process emerges from work in the 1 January *Journal of Clinical Investigation* (**115**, 168–176; 2005).

Previous studies have shown that the chemokine SDF-1 regulates aspects of stem cell behavior, such as homing to the bone marrow and adherence to bone marrow stromal cells. SDF-1 interacts with the CXCR4 receptor, which is expressed on a variety of hematopoietic cells—but the exact molecular events that occur after this interaction have remained murky. Isabelle Petit *et al*. found that SDF-1 triggered the activation of PKC-ζ. PKC-ζ was required for multiple SDF-1 mediated events, including cell polarization and adhesion to bone marrow stromal cells; conversely, overexpression of PKC-ζ enhanced motility of cells *in vitro* in response to SDF-1.

In transplantation experiments in mice, PKC-ζ was required for the engraftment of hematopoietic stem cells. What's more, injection of mice with inhibitory peptides that act as a pseudosubstrate for PKC-ζ resulted in the movement of hematopoietic progenitor cells away from the bone marrow into the blood. The results should spur research into harnessing PKC-ζ to improve mobilization regimes in stem cell transplantation.

Obedient virus

Measles virus induces cell fusion, which makes it particularly efficient at maiming tumors. But barriers to the clinical use of the virus to treat cancer remain, such as infection of non-target cells, and efforts to

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retarget viruses to cancer cells have encountered the problem of reduced efficiency of viral entry. In the March *Nature Biotechnology*, Takafumi Nakamura *et al*. make the measles virus leaner and meaner (*Nat. Biotech.* **23**, 209–214; 2005). Using a technique they had perfected with adenovirus to induce targeted cell fusion (*Nat. Biotech.* **22**, 331–336; 2004) the researchers created measles viruses that no longer bind to their native targets and instead efficiently infect tumor cells. To target tumor cells, the engineered viruses expressed single-chain antibody fragments against CD38, epidermal growth factor receptor (EGFR) or a mutant EGFR, proteins expressed on the surface of many tumors. When administered to mice with tumors bearing such surface proteins, the viruses killed the tumors or shrank them. The targeted treatment also prolonged survival in a mouse model of metastatic cancer.

The approach could be harnessed to engineer cancer-killing viruses aimed at a variety of molecular targets, an area of intensive research. For instance, Ira Bergman *et al*. recently souped up another tumor-killing virus, vesicular stomatitis virus (*Virology* **330**, 24–33; 2004). The virus steered clear of its native cellular target, expressed a single-chain antibody against Her2/neu and killed Her2/neu-expressing cancer cells in culture.

Morning madness

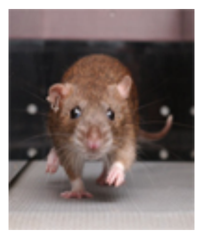
The incidence of heart attacks, stroke and cardiac arrythmias peaks at 10 a.m. That is a well-known fact long attributed to morning behaviors—such as starting work. A study in the 28 December *Proceedings of the National Academy of Sciences* (**101**, 18223–18227; 2004) explores another explanation for the pattern. Kun Hu *et al*. show that subtle fluctuations in the heart beat peak at ten a.m., and suggest that this is under control by the circadian clock.

To show this, the researchers examined five individuals cloistered over eight days in a controlled environment. The researchers first measured baseline heartbeat when subjects were kept on a 24-hour cycle of sleeping and waking; they found that the incidence of heartbeat fluctuations peaked at about 10 a.m. At 10 a.m. the beat of a healthy heart more closely resembles that of an unhealthy heart than at any other hour.

The researchers then shifted the subjects' sleep-wake pattern to a 28-hour cycle for several days. Independent of when the subjects woke up, or their level of activity, heartbeat fluctuation still peaked at around 10 a.m. Exactly how endogenous circadian rhythms influence heartbeat and whether the circadian rhythm can explain the morning spike in the incidence of adverse cardiovascular events remains to be determined.

Bred to run

Rats genetically selected to tire quickly on treadmills score high on tests for cardiovascular risk factors compared to rats bred to run without tiring. The rats selected for low aerobic capacity—who could run for 14 minutes—had higher levels of insulin resistance, blood pressure and obesity than rats with high aerobic capacity—who could run for 42 minutes. Even when they were young, and not yet fat, the low-capacity rats scored high on such measures. The findings, by Ulrik Wisløff *et al*. in the 21 January *Science* (**307**, 418–420; 2005), suggest that the low-capacity rats had metabolic syndrome, physical changes that often precede cardiovascular disease and diabetes.



University of Michigan Photo Services, Martin Vloet

The underlying defect in the low-capacity rats might originate with the mitochondria, as these rats had decreases in the levels of transcription factors that promote mitochondrial growth, such as PGC1-α. The results are in line with studies in people and animals suggesting that impaired regulation of oxidative pathways in mitochondria may contribute to cardiovascular and metabolic disease. The animals should also prove useful as badly needed models to study metabolic syndrome and cardiovascular disease.

Written by Charlotte Schubert

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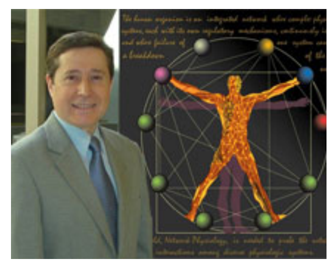

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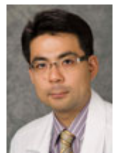
Research Round-up

Bones, Breast Cancer and Bucks: A Study on Cost-Effectiveness



Kouta Ito, MD, MS

Kouta Ito, MD, MS, of the Division of Pharmacoepidemiology and Pharmacoeconomics in the Department of Medicine, evaluated the cost-effectiveness of current screening and treatment guidelines for bone loss in postmenopausal women taking aromatase inhibitors for hormone receptor-positive early breast cancer. (Aromatase inhibitors can increase the risk of osteoporosis and related fractures.)

Ito developed a computer simulation model to project the impact of a variety of screening and treatment strategies on costs and quality of life.

Ito and fellow researchers found that annual bone mineral density screening followed by selective oral bisphosphonate therapy for women with osteoporosis was most cost-effective. However, universal bisphosphonate therapy would also become cost-effective if an anti-cancer effect of bisphosphonates is considered. The researchers suggest that future guidelines for bone fracture prevention should address the optimal use of bisphosphonates on the basis of not only their ability to prevent bone loss, but also their potential to improve breast cancer outcomes.

The study was published in the February 28, 2012, online issue of the *Journal of Clinical Oncology*.

Physiological Networks and the Body's Complex Communications

Plamen Ivanov

The human organism is an integrated network where physiological systems, each with its own regulatory mechanisms, continuously interact, and where failure of one system can trigger a breakdown of the entire network. Despite its importance to physiology and medicine, the network of physiologic interactions remains unknown.

In a first of its kind study, an international group of researchers from BWH, Israel and Germany, led by **Plamen Ch. Ivanov, PhD, DSc,** associate physiologist, of BWH's Sleep Medicine Division, may be on the path to an answer.

Over several years, the researchers developed a framework to identify dynamic interactions among diverse systems (e.g., cerebral, cardiac, respiratory, ocular and locomotor). Using sleep stages as a model of various physiological states (i.e., light sleep, deep sleep, REM), the researchers quantified a robust network of interactions.

"Each sleep stage is characterized by a specific network structure, demonstrating a clear relation between network topology and physiologic function," said **Ronny Bartsch, PhD**, BWH researcher and member of the study team.

The findings can impact clinical care. Given that multiple organ failure is a primary reason for death, this network approach may help researchers and clinicians assess whether links between physiological systems remain significantly changed even after the function of specific systems have been restored after treatment.

The study is a first step towards developing a map of communications between organ systems, and may serve as a catalyst for a new field called network physiology.

The study was published in the February 28, 2012, online issue of *Nature Communications*.

Questioning Quality of Imaging Measure

Emergency Medicine's **Jeremiah Schuur, MD, MHS,** director of quality and


Ali Raja


Jeremiah Schuur

performance improvement in the Department of Emergency Medicine, and **Ali Raja, MD**, **MBA,** associate director of Trauma, Department of Emergency Medicine, and colleagues published findings that question the reliability of a new Centers for Medicare and Medicaid Services (CMS) imaging efficiency measure.

CMS developed measure OP-15 to evaluate the emergency department (ED) use of brain CT for atraumatic headache in an attempt to improve imaging efficiency. The measure was implemented into the Outpatient Prospective Payment System in January 2012 but was never field-tested.

The researchers reviewed the CMS administrative data and medical records of 748 patients from 21 EDs in the United States to determine the reliability, validity and accuracy of measure OP-15. All the patients reviewed had been labeled by CMS as having undergone inappropriate brain CTs based on billing data.

However, when the patients' medical records were reviewed, they showed that the bills didn't tell the whole story; the researchers discovered that 65 percent of the CT scans actually complied with Medicare's measure, and another 18 percent of patients had valid reasons for the CTs documented on their charts. Overall, 83 percent of the patients should not have been labeled as having been inappropriately imaged.

This led researchers to conclude that CMS measure OP-15 may lead to inaccurate comparisons of EDs' imaging performance.

The study was electronically published February 23, 2012 in *Annals of Emergency Medicine*.

Study Finds Masks Prevent Spread of TB


Ed Nardell

In a first of its kind study, BWH researchers found that having tuberculosis patients wear surgical masks cut the likelihood of transmitting the infection in half.

"Although surgical masks have been used on patients with infectious respiratory diseases since the influenza pandemic of 1918, their efficacy has never been demonstrated," said **Ed Nardell, MD**, of the Division of Global Health Equity and principal investigator of the study. "This study is the first to quantify their effectiveness under conditions similar to real life."

The study included patients with multi-drug resistant TB who were receiving care in South Africa. Typically, care providers and other health care team members wear the masks, rather than the patients. This study tested how well it worked for patients to wear the masks to prevent TB, which is spread through droplets in the air.

"Other precautions are needed, but masks are a readily available intervention, now of proven efficacy, even in poor settings," said Nardell.

The study was published in the *American Journal of Respiratory and Critical Care Medicine*.

Turn Off Protein, Turn On Lung-Healing

Researchers from BWH and the University of Melbourne, Royal Melbourne Hospital in Australia, have identified that serum amyloid A plays a key role in chronic inflammation and lung damage in chronic obstructive pulmonary disease (COPD) and also inhibits the natural effort of the lung to repair itself after smoking has stopped. The discovery could lead to the development of a new treatment strategy with lipoxin stable analogs (synthetic forms of a natural healing agent) to boost lung-healing. This new approach could also improve the effectiveness of steroid treatment for COPD, which is effective in treating other lung diseases such as asthma. It is hoped the new treatment will go to clinical trial within the near future.

The study is published in the *Proceedings of National Academy of Science*.