

THE SCIENCE CREATIVE QUARTERLY ISSUE ONE PART TWO OF SIX APRIL 25TH 2005 WEEEEEEEEEE!

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Our masthead is still evolving, although at present we have two Daves, a Bethany, a Caitlin, a Stephen, a Claire, a Russell and also an exotic sounding Azar.

In addition, we think that Chris and his friends are interested.

Want to participate? Check out our submission guidelines at <http://bioteach.ubc.ca/quarterly/submissions.html>

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THIS TIME AROUND



Dear Reader,

It appears that within this second part, we have many articles of the “sex, drugs and rock ‘n’ roll” vein. For this, we apologize profusely, and offer that in no way is this a pathetic attempt at garnering more readers (although curiously enough, the “boobie” piece from the previous issue did in fact receive the most traffic). In any event, we hope that our inclusion of an article about hot dogs will present a more well rounded experience for those discerning readers

SWEATY SEX

BY BETHANY LINDSAY

Cameron Muir thinks a lot about hot, sweaty sex.

It's his job, after all. Muir is a psychologist at Brock University, and his current fascination is human sweat — particularly when it's coitus-induced.

His interest in sweat was aroused by steroid hormones, the tiny molecules like testosterone and estrogen that control so much of human sexuality from the inside of our bodies. Testosterone, in particular, can profoundly change a person's appetite for sex.

Women who have had their ovaries removed often complain they've lost their libidos, probably because of changes in hormone concentrations. "They'll go to the doctor and say I'm married, I have no sex drive, and my husband doesn't like it," said Muir. "What the doctor will do is prescribe testosterone."

The testosterone usually comes in a cream that women rub on their bellies—steroid hormones are small enough to be absorbed through the skin.

The treatment started Muir thinking. What if he could find a natural version of testosterone cream in men's armpit sweat? Sure enough, he discovered that when men vigorously exercise, they did indeed sweat out small amounts of testosterone.

Furthermore, when that exercise is sex, they excrete much higher amounts of the hormone. "The concentration is more than

ten times higher, and that concentration is almost as high as the concentration doctors would prescribe for women to enhance the libido," said Muir.

All of which suggests to Muir that testosterone may act as a pheromone in humans. "During sweaty sex, a man might transfer his testosterone to the female, turning her on even more," he said.

More importantly, his findings and theories are helping revive the decades-long debate about whether human pheromones even exist.

Pheromones act as silent messengers between animals—they are molecules that are secreted by one animal and perceived by chemical receptors in another.

"When you see a dog sniffing a fire hydrant, he's not smelling it per se, but he's getting information about who was there recently, and what kind of state they're in," said Muir. "Is there a dog in heat around here? Is there a dog defending its territory?"

Whether pheromones are at work in humans is another matter. Martha McClintock, now of the University of Chicago, did the first study on human pheromones when she was an undergraduate science student in 1971. She observed how the menstrual periods of the women in her dorm slowly became synchronized, and suggested that a pheromone in their armpit sweat was responsible.

Her research remains contentious. Scientists agree that her methods were sloppy, and some detractors still use her study's shortcomings as an argument against human pheromones.

Unreliable methods continue to haunt pheromone researchers, and the financial interests of some of their colleagues aren't doing anything to raise the reputation of the field.

The Athena Institute in Pennsylvania is a leading producer of human pheromone research. They claim to have discovered pheromones that make men and women go wild for each other and they've published their results. But the results can't be replicated in other labs because the formulas of the pheromones are secret—and the Institute sells them in vials on the Internet.

Muir says the biggest debate in the human pheromone controversy is about where humans receive pheromonal messages. For most animals, pheromone receptors are in something called the vomeronasal organ—the organ at the back of a snake's mouth that she touches her tongue to in order to “smell” her surroundings

“The vomeronasal organ is well understood to be involved in transmission of chemicals from one animal to another,” said Muir. “Humans do have a vomeronasal organ, but it doesn't seem to be functional. “

But there is mounting evidence that mammals send and receive chemical cues. An American study in the journal *Nature* last month identified a new mouse pheromone. The researchers also zeroed in on the receptors that accept the pheromone's message—they're in the olfactory bulb, the organ responsible for smelling, and not the vomeronasal organ. A similar system is possible in humans.

Muir's research indicates a third receptor for pheromones, beyond the vomeronasal organ and the sense of smell. Steroid receptors beneath the skin might be all that's needed for

human pheromone transmission.

“We don't need a vomeronasal organ. If you can drip sweat bursting with testosterone onto a female's belly during sex, this might explain what's going on,” said Muir.

He now wants to look at a distinctly human behaviour—kissing, which is often a precursor to sex. The human mouth is full of testosterone receptors, and Muir wonders if there's a high concentration of testosterone in saliva. “Why would you have steroid receptors in your mouth if it weren't for a reason like this?”

Muir is also concerned that his studies reflect a common bias in sex attraction research that says males are the only sex competing for mates—most human pheromone research focuses on how men can attract women, not the other way around. Muir hopes to help correct this, and begin research that would look at how women use chemicals to turn men on.

There is already some research into how men react to steroid hormones, which can also be inhaled in high concentrations. A European team has found that men who are sprayed with estrogen will confuse male and female faces—effeminate men start to look like women. Another group has shown that homosexual men (and heterosexual women) prefer chairs that have been sprayed with testosterone.

Muir expects that the skepticism over human pheromones will keep the pace of research moving at slug speed. To support his pheromone studies, he has been forced to divert money from other projects.

“I just can't seem to get funding for this research,” said Muir, “I'll hand in my grant

application, and one referee will say 'you're right, this is great' and the other referee will say, 'I'm sorry no, I don't believe in human pheromones,' and you have to have both of them to get the grant."

RANK: ANIMAL ILLNESSES

BY CLAIRE ZULKEY

Chicken Pox.

This is the Frank Sinatra of animal-themed sicknesses. A timeless classic, although the younger generations might not appreciate it. I remember fondly going to a Fourth of July Parade as a child, just recovering from the pox, and my mom not letting me look around too much lest other parents see my pox and get upset for contaminating everyone else. I also have a few choice scars from the ol' poxy. Drawback: Some children are getting 'vaccinated' for this. Wimps.

Avian flu.

While this is the hot disease of the moment, it still can't measure up to the granddaddy, pox del pollo. I don't know much about this disease other than that I saw a Chinese man piling handfuls of live chicks into garbage bags on "Today," so I think it's gross. Downside: While I don't really care about full-grown poultry, I'm never happy to see cute baby chicks fall ill with the flu. Do they get little bowls of vegetarian chicken soup?

Monkey pox.

This was the disease du jour a few summers ago, but I think that most people just liked saying "Monkey Pox," and maybe imagining a sad little chimp with a heating pad and tiny thermometer, than really knowing what the disease was about. Downside: Things are sad on the planet of the apes.

Prairie dog pox.

This was a form of monkey pox passed on by pet prairie dogs, and what I want to know is, who has pet prairie dogs and where can I get one? For scientific research, of course. And oh yes, terrible about the disease, just terrible. Downside: Too many syllables.

CARTOON FEATURE: EINE KLEINE ZELLE

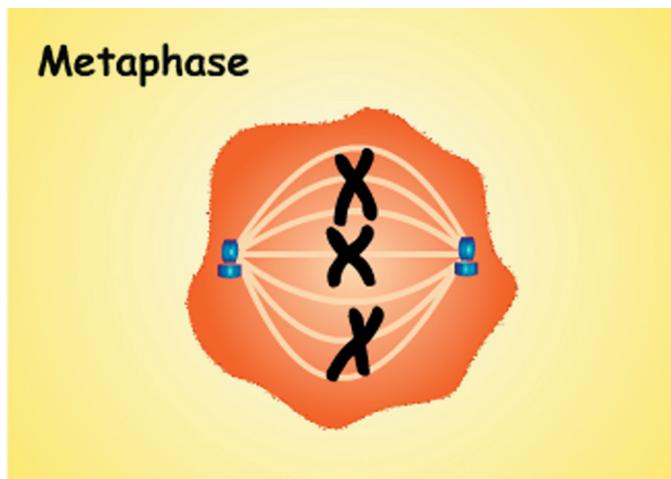
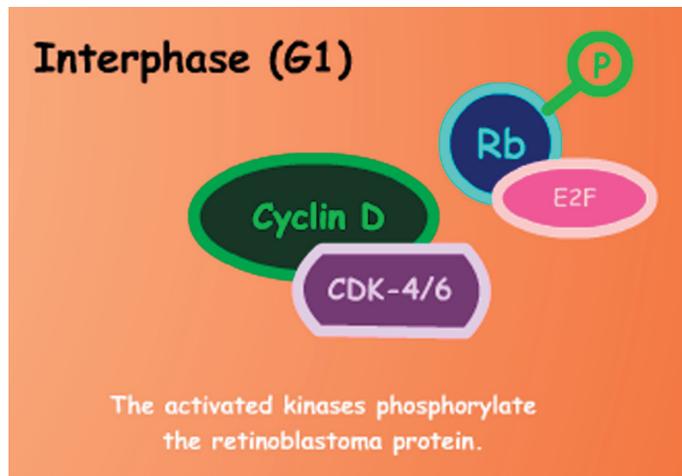
BY CORINNE HOESLI



A small cell, alone in the world, in the republic of cells..

The basic structure of life would not be nearly as interesting if it weren't for its ability to create more cells. If you think the "random" separations between cell cycle phases are about as tenuous to remember as the first 30 digits of Pi, then you probably haven't seen a cell shake its booty to the Pink Flamingos in a Fritz Langesque vignette yet.

(flash file with audio,
go to
<http://bioteach.ubc.ca/quarterly/>)



HALF BAKED SCIENCE: A PRIMER ON MEDICINAL CANNABIS

BY RYAN N. PHILLIPPE
IMAGE BY JEN PHILPOT

Cannabis (marijuana) is among the most widely used of all psychoactive drugs. Despite the fact that its possession and use is illegal in most countries, cannabis is used regularly by as many as 25 million people in North America and Europe and by millions more in other parts of the world. There has been renewed interest in the potential medical uses of cannabis (*Cannabis sativa*) in recent years, with voters in several areas of Canada strongly supporting such a move. Opinion polls suggest similarly strong popular support for the reintroduction of medical cannabis in the USA, the UK, and many European countries. Expert reviews of medical and scientific evidence on this topic carried out on both sides of the Atlantic in the past few years have encouraged further clinical and scientific research [1-3]. This paper seeks to give a brief review of the scientific facts, ranging from the botany of the cannabis plant and the biochemistry of the receptors it binds, to the potential uses of the plant for medicinal purposes.

The Plant

Cannabis is one of the very oldest of economic plants, providing fiber, edible seed, and drug resin. The plant likely originated in Central Asia or near the Altai or the Tian Shan mountains. It was first cultivated in China, followed shortly by cultivation in India [4]. Human selection for various uses and natural selection pressures imposed by diverse climates has resulted in a wide variety of growth forms and chemical compositions. Innovative classical breeding techniques have been used to improve drug cannabis, resulting in many cannabinoid-rich cultivars suitable for medical use. The production of cannabinoids is unique to Cannabis, and cultivars with specific chemical profiles are being developed for diverse potential pharmaceutical uses. Cannabis is an annual plant, propagated from seed or vegetative cuttings, and it grows vigorously in open sunny environments as part of its natural life cycle. In light, well-drained soil with ample nutrients and water, the plant will reach up to 5 metres in height in a four- to six-month growth season. Feral Cannabis populations are frequently found in association with human habitation. Agricultural lands, roadsides, exposed riverbanks, meadows, and disturbed lands are ideal habitats for wild and feral Cannabis, as they provide adequate sunlight [4].

Seeds usually germinate in three to seven days. During the first two to three months of growth, juvenile plants respond to increasing day length with more vigorous vegetative growth and new leaf development. Later in the season (after the summer solstice), shorter days (actually, longer nights, if you consider how the photoperiodic effect is monitored) induce flowering and complete the life cycle. Cannabis begins to flower when exposed to short day lengths of 12 to 14 hours or less (long nights of 10 to 12 hours or more) depending on its latitude of origin. How-

ever, a single evening of interrupted darkness can disrupt flowering and delay maturation. If an individual plant is not crowded by its neighbours, as in the case of crops intended for seed or drug production, flower-bearing limbs will grow from small buds located at the base of the leaf petioles originating from nodes along the main stalk [4].

Cannabis is normally a dioecious plant, with male and female flowers developing on separate plants. The sexes of Cannabis are anatomically indistinguishable until they begin flowering. However, Mandolino and Ranalli report success using RAPD analysis to identify male-specific DNA markers, to separate out the two sexes before fertilization can occur [5]. The development of male and female plants varies greatly. The male flowers hang in loose clusters along a relatively leafless upright branch. In contrast, the female plant has very crowded clusters of individual flowers at the base of each leaf along a branch. Male Cannabis flowers require air currents to carry pollen grains to the female flowers, which results in fertilization and subsequent formation. The male plants finish shedding pollen and die before the seeds in the female plants ripen 4-8 weeks after being fertilized. The singleseed in each female flower ripens in 3-8 weeks and will either be harvested by humans, eaten by birds or rodents, or it will drop to the ground. A large female plant can produce over one kilogram of seed. This completes the natural four to six month life cycle. If birds or rodents do not consume the seeds, they may germinate the following spring. Cannabis seeds are a balanced source of essential fatty acids, and easily digestible protein. They are usable as human food or animal feed. These essential fatty acids have also been shown to have many important physiological roles and hemp seed oil is a valuable nutraceutical [6].

Much of the Cannabis presently used for medical purposes is grown indoors under artificial lights. Metal halide and sodium vapour light systems are most often set up in attics, bedrooms, or basements. Most modern indoor growers produce vegetatively propagated crops, meaning they are grown from cuttings rather than from seeds. Only female drug Cannabis plants are economically valuable and garden space is often limited. In addition, the legal systems of many nations penalize growers of large quantities of cannabis with harsher penalties. Therefore, under artificial growing conditions, crops are reproduced vegetatively by planting root cuttings of only female plants, or by transplanting and inducing flowering almost immediately. Cuttings taken from one plant are genetically identical copies of a single plant and they should all respond in the same way to environmental inputs. Given that environmental influences are constant, the clones will yield a uniform crop of nearly identical seedless females. Under ideal conditions, yields of dried floral clusters can reach 1,200 grams per square meter per year if three to five crops are grown per year [4].

The psychoactive component of cannabis, D₉-THC (D₉-tetrahydrocannabinol), is produced in resin glands that adorn the surface of Cannabis leaves. When resin gland development commences, the medically important cannabinoids and the associated aromatic terpenoids begin to appear. Solitary resin glands most often form at the tips of slender stalks which form as extensions of the plant surface. The cluster of one- or two-dozen head cells atop each stalk secrete aromatic terpenoid-containing resin with a very high percentage of cannabinoids (> 80%), which collects under a thin waxy membrane surrounding the secretory head cells [7]. The secreted resin component is,

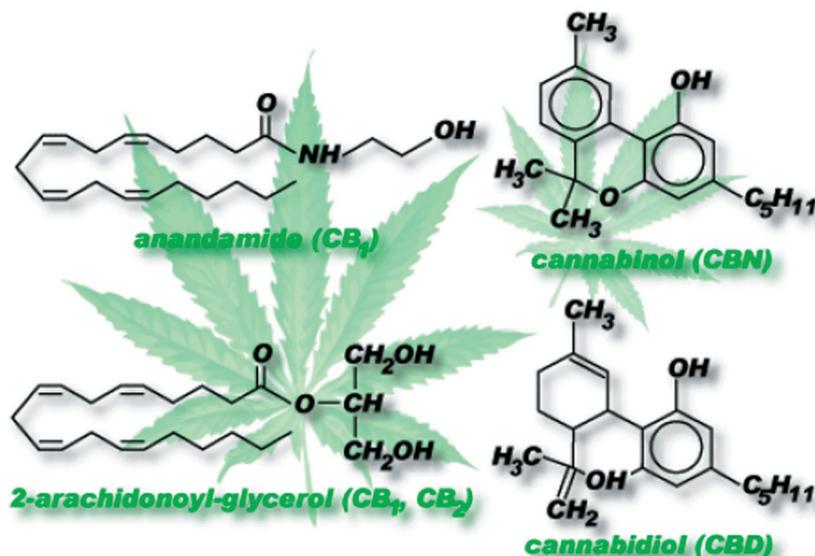


Figure 1. Some examples of endogenous (left) and exogenous (right) cannabinoid receptor ligands.

in large part, segregated from the secretory cells. This isolates the resin from the atmosphere as well as membrane-bound enzyme systems within the secretory cells, possibly protecting the terpenoids and cannabinoids from oxidative degradation and enzymatic change. Resin glands containing cannabinoids and terpenoids may have an adaptive significance for the Cannabis plant as defense against environmental challenges, including insect attack or drought [8]. However, Cannabis crops are still subject to infestation by a wide variety of pests, particularly under greenhouse or grow-operation conditions. The intoxicating effects of this Cannabis resin have increased cannabis consumption by humans, as well as encouraged its domestication, thus dramatically widening the distribution of the plant.

Cannabinoid Receptor System

Because psychotropic cannabinoids have high lipid solubility and low water solubility, they were long thought to owe their pharmacological properties to an ability to perturb the phospholipids constituents of biological membranes. Although this mode of action cannot be excluded altogether, it is now clear that for many of the effects of cannabinoids, the predominant underlying mechanism is far more specific. It is now known that cannabinoids act through receptors: CB1 receptors (cloned in 1990), and CB2 receptors (cloned in 1993) [9]. Both of these receptor types are coupled through G proteins, negatively to adenylate cyclase and positively to mitogen-activated protein kinase. In addition, CB1 receptors are coupled to ion channels through G proteins, negatively to calcium channels and positively to potassium channels. CB1 receptors also mobilize arachidonic acid and close receptor ion channels [10].

CB1 receptors are found in particularly high concentrations within the central nervous system (CNS). However, they are also present in certain peripheral organs and tissues. These include some neurons and endocrine glands, leukocytes, spleen, heart, and parts of the reproductive, urinary, and gastrointestinal tracts [9]. Some CB1 receptors are located at central and peripheral nerve terminals where they probably modulate neurotransmitter release when activated. Although the concentration of CB1 receptors is considerably less in peripheral tissues than in the central nervous system, this does not imply that peripheral CB1 receptors are not important. Some peripheral tissues may contain high concentrations of CB1 receptors, localized in discrete regions such as nerve terminals that form only a small part of the total tissue mass.

Within the CNS, the distribution pattern of CB1 receptors is heterogeneous and can account for several prominent pharmacological properties of CB1 receptor agonists (a chemical that can combine with a receptor on a cell to produce a physiologic reaction typical of a naturally occurring substance). For example, evidence shows that the cerebral cortex, hippocampus, and basal ganglia (areas of the brain involved in learning and thinking) are richly populated with CB1 receptors and that these receptors mediate the well-documented ability of CB1 receptor agonists to impair cognition and memory and to alter motor function [9]. CB1 receptor agonists are also analgesic, and in line with this property, there is evidence for the presence of CB1 receptors in several areas of the CNS that mediate the perception of pain [11].

CB2 receptors are expressed primarily by immune tissues, for example leukocytes, spleen and tonsils [9]. More mRNA for CB2

than CB1 receptors exists in the immune system, and the level of CB2 mRNA in human tonsils matches that of CB1 mRNA in human cerebellum. Levels of CB1 and CB2 mRNA in human immune cells have been shown to vary with cell type [11]. CB2 mRNA has not been detected on neuronal tissue from human or rat brain. In contrast to the CB1 receptor, the physiological roles of CB2 receptors are proving very difficult to determine.

The discovery of cannabinoid receptors was followed in 1992 by the demonstration of the existence of endogenous cannabinoid receptor agonists [12]. The most important of these are arachidonylethanolamide (anandamide) and 2-arachidonylglycerol (2-AG), and there is evidence that both of these compounds can serve as neuromodulators or neurotransmitters. This belief comes from demonstrations that they are synthesized by neurons, that they can undergo depolarization-induced release from neurons and that once released they are rapidly removed from the extracellular space [12]. For anandamide, such removal occurs when neurons take the chemical up into the cell from the extracellular space. Once within the cell, anandamide is presumably degraded to smaller signaling compounds that will elicit a physiological effect. Cannabinoid receptors and their endogenous ligands together constitute what is now often referred to as “the endogenous cannabinoid system.” Current research is exploring the role of the endogenous system in the human body. Hypothesized functions, based on the location where the cannabinoid receptors are found, involve learning, memory, appetite, reproduction, and immunity. Much more work remains to be done in this rapidly expanding field.

Medicinal History

One of the first crops to be cultivated by mankind, cannabis use is as old as agriculture. First grown for its fibres, the ancient Chinese used it to make rope, cloth and even paper. One of the world's first pharmacy books, the Pen Ts'ao, published in China around 2800 BC, recommends hemp as a remedy for just about everything- including, ironically, absentmindedness. The earliest references to its psychoactive properties appear in the Atharva-Veda, a sacred Indian text dating back to 2000 BC [13].

It was probably the Scythians, a barbaric tribe from the Caucasus, who introduced the plant to Europe. The Greek traveler Herodotus (circa 500 BC) wrote of the Scyth warriors purifying themselves in steam baths filled with smoke from burning hemp seeds:

"They make a booth by fixing in the ground three sticks inclined toward one another, and stretching around them woolen pelts which they arrange so as to fit as close as possible: inside the booth a dish is placed upon the ground into which they put a number of red-hot stones and then add some hemp... immediately it smokes and gives out such a vapour that no Greek steam bath can surpass it... the Scyths howl with pleasure at these baths."

Herodotus' claims were recently born out by archaeological finds of tripods, braziers and hemp seeds in frozen Scythian tombs in central Asia [13].

The Greeks and Romans cultivated hemp for its fibres, seeds, and medicinal applications, although there are a few references to its use as a social lubricant at banquets "to promote hilarity and enjoyment". Throughout the Middle Ages and into the Elizabethan era, hemp was grown in Europe and in Britain,

where it fulfilled the massive demand of the British Navy. While the therapeutic properties of cannabis were being all but ignored by the Europeans, in India, entire systems of medicine were being built up around it. The herb's intoxicating effect was very closely tied to its medicinal use. Because of its psychoactive properties it was prized more than ordinary medicines. It was prescribed for a variety of ailments, including headaches, mania, insomnia, rheumatism, menstrual pain and tuberculosis [13].

W.B. O'Shaughnessy, a surgeon with the British East India Company, and professor at the University of Calcutta, introduced cannabis to modern Western medicine. In 1839, after investigating its use in India and validating many of its applications, he documented its properties as an analgesic in the treatment of rheumatism, and as a remedy for severe convulsions. His contemporary, Jean Joseph Moreau de Tours, a French psychologist, proposed using cannabis as a means to treat mental illness. Interest in cannabis as a medicine spread from Europe to America, and very quickly preparations of cannabis became widely available. The famous physician Sir John Russell Reynolds prescribed it to Queen Victoria for menstrual cramps. Needless to say, its intoxicating nature didn't remain a secret for very long, and many artists and intellectuals of the time readily embraced it [13].

Until the early twentieth century, cannabis was legal and found common use as an everyday medicine. Doubts about the drug began to surface when, at the Second Annual Opiates Conference in 1924, an Egyptian representative complained that workers preferred to lie around smoking hashish than do anything constructive. In 1925, the Dangerous Drugs Act became law, and non-medicinal cannabis was made illegal

in Britain. Canada followed suit and banned all forms of cannabis in 1927. Finally, in 1937, with 28 cannabis pharmaceuticals on the American market, the US government effectively criminalized cannabis by passing the Marihuana Tax Stamp Act [13].

Modern Medicinal Applications

The recently revived interest in the medical uses of cannabis arose at least partly from its popularity as a recreational drug in the 1960s and 70s. Anecdotal reports from young cancer patients who used cannabis reported that it relieved the nausea and vomiting caused by chemotherapy treatments. Modern chemistry also brought about increased interest in the use of at least one of the constituents of cannabis, when Goani and Mechoulam isolated and synthesized D₉-THC in 1964 [14]. This made the clinical testing of D₉-THC during the 1970s and 80s possible, and eventually resulted in the official approval and marketing of the compound as a prescription drug. The chemical synthesis of D₉-THC also made possible the synthesis and clinical testing of an entirely new class of pharmaceutical compounds, the synthetic cannabinoids.

Dronabinol is another name for the synthetically manufactured (-)-trans-isomer of D₉-THC, which is often mentioned in a medical context in scientific literature. Marinol is a trademarked dronabinol preparation dissolved in sesame oil in capsules. It is a registered trademark of Unimed Pharmaceuticals, Inc. It is available in Canada, the USA, and the UK [15]. However, dronabinol has a relatively high incidence of side effects, particularly anxiety and depression. Nabilone is a synthetic derivative of D₉-THC with a slightly modified molecular structure. With regard to pharmacological activity, 1

mg of nabilone corresponds to about 10 mg of dronabinol. It is a registered trademark of Eli Lilly & Co., and marketed under the name Cesamet. It is on the market in Canada and the UK, and some other European countries [15]. The Pfizer compound levonantradol was tested in several clinical trials during the early 1980s. It proved to be considerably more potent than morphine as an analgesic, and was effective in blocking nausea and vomiting in patients undergoing cancer chemotherapy. Nevertheless, the psychoactive side effects proved to be unacceptable and the company decided to abandon further research on this project [16]. Other synthetic cannabinoids have been developed with applications relating to research, due to undesirable side effects. Research continues into the development of synthetic cannabinoids that can provide therapeutic benefits while minimizing the medically undesirable psychoactive side effects.

Cannabis preparations and synthetic cannabinoids have been employed in the treatment of numerous diseases, with marked differences in the available supporting data. For applications such as nausea and vomiting associated with cancer chemotherapy, anorexia and cachexia in HIV/AIDS, and spasticity in multiple sclerosis and spinal cord injury, there is strong evidence for medical benefits. For indications such as epilepsy, movement disorders, and depression, much less data is available. However, the history of clinical use of cannabis and cannabinoids has demonstrated that the scientific evidence for a specific indication does not implicitly reflect the actual therapeutic potential for a given disease. Clinical studies with single cannabinoids (like dronabinol), or, less often, with whole plant preparations (smoked cannabis or cannabis extract), have often been inspired by positive anecdotal experiences of patients

employing crude cannabis (often illegally). The antiemetic properties, appetite enhancing effects, relaxing effects, and therapeutic use in Tourette's syndrome were all discovered (or rediscovered) this way.

Movement and spasticity disorders

In small clinical trials of THC (dronabinol), nabilone, and smoked cannabis, a beneficial effect on spasticity caused by multiple sclerosis or spinal cord injury has been observed [17]. Among other positively influenced symptoms were pain, paraesthesia (tingling skin), tremor, and ataxia (uncoordinated movement). In folk medicine there are also report of improved bowel and bladder control. Some anecdotal evidence for the benefits of marijuana in spasticity due to central lesions also exists [18].

There are some positive anecdotal reports of therapeutic response to cannabis in Tourette's syndrome, dystonia ('frozen' muscles), and tardive dyskinesia (jerky, flailing movement). The use of the drug in treating Tourette's syndrome is currently being investigated in clinical studies. Many patients experience a modest improvement; however, some show a considerable response or even complete symptom control. Cannabidiol, another natural cannabinoid found in Cannabis, produced a 20 to 50 percent improvement in five patients with dystonia. In Multiple Sclerosis patients, improvements to ataxia and reduction of tremor have been observed following the administration of THC [19]. Despite occasional positive anecdotal reports, no objective success has been found in Parkinson's or Huntington's diseases.

AIDS

In addition to a mountain of anecdotal patient-reported evidence, the appetite-enhanc-

ing and nauseasuppressing effects of THC have also been observed in clinical trials. In a long-term study of 94 AIDS patients, the appetite-stimulating effect of THC continued for months [18]. Patients tended to retain a stable body weight over the course of seven months, instead of succumbing to the wasting syndrome associated with AIDS. However, the slow onset of action of oral THC, and its high cost and high incidence of side effects, result in many patients preferring herbal cannabis. In addition, some people report better symptom control with cannabis rather than dronabinol, which may be related to the additional cannabinoids, such as cannabidiol, that are found in natural cannabis but not in dronabinol. Unfortunately, the potential respiratory damage resulting from smoke inhalation is at odds with the reduced efficacy of the AIDS' patient immune system. Harm reduction research indicates that heating cannabis to temperatures well below combustion ("vapourization") yields active cannabinoids with a significant reduction or elimination of the toxic compounds commonly found in cannabis smoke. More research is required but vapourizers appear to substantially reduce what is widely perceived as the leading health risk of cannabis [20].

Cancer

Cannabis can act an appetite stimulant, and "generally improves the quality of life" of terminal cancer patients by helping with pain, nausea, vomiting, and loss of appetite associated with chemotherapy [21]. Treatment of pain and of the side effects associated with chemotherapy is the medical indication for cannabinoids that has been most frequently documented. About 40 studies involving THC (dronabinol, nabilone, other THC analogues, smoked cannabis) have been performed. Most trials were conducted in the 1980s. Oral THC has to be given in

high and frequent doses, therefore resultant side effects may occur more frequently than with other drugs.

Pain

Few clinical studies of cannabinoids' effects on pain exist. In two trials, oral THC proved to be effective against cancer pain. However, some patients experienced intolerable side effects. In a single-case double-blind study a patient with recurring pain clearly reduced his need for opiates while receiving THC in comparison to placebo [18]. According to reports from pain therapists, the use of opiates and cannabis concurrently appears to be promising, particularly since cannabis does not cause respiratory depression (as opiates can). Cannabis has been used successfully in modern folk medicine to treat a multitude of painful conditions, such as migraine and other forms of headache, musculoskeletal disorders, arthritis, rheumatism, ulcers, Crohn's disease, and menstrual pain.

Medical Possibilities

Cannabis-based medicines have been used for thousands of years in Asia, and were popular for 100 years in Western medicine after their introduction in the mid-nineteenth century. They fell out of use largely because of the difficulties that physicians encountered in obtaining consistent results from batches of plant material of varying potency. Patients consequently suffered from either treatment with an ineffective dose or the unwanted intoxicating effects of an overdose that could last for many hours. Modern techniques of plant breeding and cultivation have undoubtedly solved the problem of quality control in the use of herbal cannabis as a medicine, but the issue of a narrow therapeutic window between the desired benefits and the usually unwanted psychoactive effects remains a challenge.

Many scientists would argue that modern medicines should be single chemical entities wherever possible, rather than complex mixtures of plant constituents. Proponents of herbal cannabis assert that the plant material has advantages over the pure cannabinoid D9-THC. This argument is often confused, however, by the fact that herbal cannabis is usually smoked whereas THC is taken orally. The oral route for THC is notoriously slow and unreliable, whereas smoking is a very efficient way of delivering the drug quickly and in a manner that allows flexible dose control [18]. Smoking, however, carries medical risks. In the short term, the irritant effects of cannabis smoke can lead to bronchitis. In the long term, there is the potential for increased risk of cancers of the lung, airways, and mouth. Although the cancer risk cannot be accurately quantified as yet, it may be one of the most serious potential dangers of cannabis [20]. Better methods for delivering both herbal cannabis and pure THC are urgently needed; perhaps vapourization will prove to be an effective and safe mode of administration. Although there have been suggestions that cannabis has adverse long-term effects on pregnancy, the immune system, fertility, and cognition, the available evidence suggests that these are far less severe than originally thought [16].

The 1990s witnessed major advances in our scientific understanding of how THC and other cannabinoids act on the central nervous system. The discovery that the brain and other organs contain specific protein receptors that recognize the drug and trigger cell responses is analogous to the discovery in the early 1970s of opiate receptors in the brain that bind morphine and other opiates. As with the opiates, the discovery of specific cannabinoid receptors prompted the search for putative naturally occurring chemicals

that interact with the receptors. This led to the discovery of anandamide as the first of the naturally occurring endogenous cannabinoids. Although anandamide belongs to an entirely different chemical class than THC, it is bound by the same receptors. These discoveries shed entirely new light on the pharmacology of cannabis. Exploration of synthetic anandamide-like chemicals may be one way to obtain improved cannabinoid-based medicines. The pace of discovery has been so rapid in recent years that it would not be unreasonable to anticipate that more members of the cannabinoid receptor family and additional endogenous cannabinoid substances may yet be discovered in the future. This, in turn, could lead to new therapeutic opportunities, perhaps involving a number of natural cannabinoids that do not bind known cannabinoid receptors but nevertheless have some important pharmacological effects.

When cannabis medicines disappeared over half a century ago, this was not perceived in most medical circles as a major restriction of the therapeutic arsenal. However, the situation today is somewhat different. Modern cannabis research and traditional usages along with modern anecdotal reports indicate that cannabis may be the drug of choice for certain patients and conditions. The future will demonstrate whether cannabis in a medicinal context must forever remain a subject for historians.

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HEY BABY! I THINK OUR INTERACTION FUNCTIONS WOULD MESH WELL. LET'S DATE.

by Clive Glover

(A review of research by Dr. John Gottman at the University of Washington: "A General Systems Theory of Marriage: Nonlinear Different Equation Modeling of Marital Interaction". J. Gottman, C. Swanson, K. Swanson. Personality and Social Psychology Review: 6(4), 326-340, 2002).

ABSTRACT:

This article describes a new mathematical approach for modeling the prediction of divorce or marital stability from marital interaction using nonlinear difference equations. The approach is quite general for modeling social interaction, and can be applied to any time series data generated over time for two individuals. We pursued a balance model in selecting the dependent variables of this modeling. Both the mathematical methods and the theoretical gains obtained when using this approach are reviewed

It's happened to many of us in the relationships we are part of - we make an idle comment to our other halves and five minutes later, an all-out battle is ensuing which threatens all known modes of normality. Of course, we've also all seen those cutesy-wutesy couples that wander around holding hands constantly, whispering sweet nothings to each other. And, we can all sigh, wonder at the mystery of relationships, and question why some work out and others just don't.

Well, you'll be pleased to know that scientists at the University of Washington have claimed that after watching a couple interact for as little as 30 minutes, they have a 90% chance of predicting whether the relationship will last.

To take all the mystery out of it (or maybe add some of the mystery back in, depending on your perspective), one of the tools that they use are a class of mathematical modes called difference equations. In this case, the difference equations are used to model the effect of one of the partner's comments on the behaviour of the other. The behaviour, which is assessed through a combination of physiological signals as well as simple stances and replies, is tracked through the course of a carefully controlled interaction between the couple. This observation leads to the prediction of an "interaction function" for each member of the couple and, through a series of mathematical manipulations, these "interaction functions" can be converted into two nullclines or lines which predict the state at which that individual's behaviour will not change, assuming that the other partner's behaviour remains constant.

For example, let's assume that your mood has some influence on your partner's (hopefully this is a valid assumption), and that the researchers can somehow control your mood so that it does not change. According to the assumptions of this model, your partner's mood will reach some state which will be dependent on your mood. If the researcher's change your mood, your partner's will too and will reach another steady state. If we look at a continuous graph of all your moods and plot your partner's against that, the line that is formed by joining up all the points will be your nullcline. The same thing can be done the other way around where your partner's mood can be experimentally manipulated and your final resting mood observed.

Now comes the key point about the models predictability. Where the two nullclines cross is what mathematicians call a steady state. This is a point where if each member of the couple starts on that exact mood predicted by where the nullclines cross, and assuming that there are no external influences, they will stay at that point no matter how long the interaction between them takes place.

There are two types of steady states: stable ones and unstable ones. Think about steady states as the tops of hills or the bottom of valleys: if a ball is placed at the very top of a hill or the very bottom of a valley, it will stay there forever as long as nothing forces it to move. However, the behaviour of the ball, if it is moved slightly will vary drastically depending on whether it is on the hill or in the valley. The same thing applies for the relationship steady states. If a couple's nullclines cross in such a way that they form a stable steady state, no matter how they get emotionally pushed, they will return to a good interaction and both partners will be happy. However, if they cross in such a way that they have an unstable steady state, things do not look too good and the divorce lawyers might as well be lining up outside the door.

Interestingly, by understanding the factors that make for really happy relationships, researchers are able to teach bad relationships to get a little better, but, unfortunately, this is only a temporary improvement. Long term improvement can only come by changing the couple's nullclines which, presumably is heavily influenced by the personalities involved and so would take drastic change on the part of the individual.

Of course, with all the current debates raging around much of the western world about what marriage really means, one wonders if a 30 minute session with one of the UW researchers would make any further debate a moot point.

PARENTS AS A NARCOTIC

BY RUSSELL BRADBURY-CARLIN



Last weekend, Candace, Will and I visited my mother. And, while I was there, I realized I was very tired. Granted, I had not slept well the night before, but it suddenly occurred to me that I am often tired when I visit my mother. Then, on the way home, it also occurred to me that I often feel tired when Candace and I visit her father or mother. I brought this up to Candace. I asked her if she thought I had some kind of problem. “Have I developed a mental association with our parents...some self-imposed Pavlovian condition...is it my way of checking out around them?” Candace, defending me from myself, offered another perspective - “maybe you just relax when you visit our parents. You know, kind of like going back to your childhood home. You don’t have any obligations or chores like at home. You chill.”

Good, I thought. Then I realized that our eight month old son often seems tired. He certainly sleeps a lot - three solid naps a day and he snoozes through most of the night. He can barely keep his eyes open after two hours around us. Then I thought about all of the other parents that I know. And, you know what? Their babies sleep a lot, too. And when we get together with these parents all we talk about is how tired we are.

I am beginning to suspect that its not babies that make parents exhausted...its themselves. It is us.

If my supposition is true, parents are a sedative, even to themselves. We (or at least I) get sleepy around our parents, our children get sleepy around us, and we get sleepy around other parents. In fact, for the last eight months all I’ve talked about is how tired or not tired I am (usually the former). My daily condition is based on this. But, I’ve been eyeballing the wrong culprit. It is not Will. It is myself.

I wonder if babies were left to their own devices if they would stay up all day like a “normal” human being. Maybe that’s the way it should be. We let the babies hang-out and play with each

other all day, while we parents hang-out with ourselves and breath in the sweet sedative that is us. Then we could all curl up on the floor, like in kindergarten (maybe they used to keep a stash of parents in the closet so we'd get tired at "nap-time"). It certainly would be nice to give into the red-eyed junky-demon that is exhaustion sometimes.

The more I think about it, the more this makes some kind of wicked sense. All of my older friends who suffer from insomnia either don't have children or their children have grown up and moved on. Perhaps the sedative-effect only occurs while you are actually parenting.

You know, I could rent out parents to insomniacs. I could set up sleep clinics where those who suffer from sleep disorders are administered three or four parents a night until they can return to restful nights or sleep. Or I could even create a Parent Channel that features a line of parents jumping over a fence like sheep to help those who need a little assistance to drift off. Yeah, that's it.

Besides, who likes warm milk anyway.

WHITE LADY

BY P.Z. MYERS

The animal I've been working with in my class lately is the beautiful beastie, *Drosophila melanogaster*. While I was cleaning out some stocks, I found this lovely example, a pale lady.



She is a white mutant, and so lacks the normal red pigment in her eyes. In addition, she had just recently eclosed from her pupal case, and although her wings looked neat and pressed, her cuticle hadn't yet fully tanned. She looked even more ghostly when I first spotted her, and was visibly darkening as I put her under the camera.

Here's a close-up. It's amazing how every hair has its place, and she looks so neat and trim and glossy. Every hair has a nerve or nerves, and is a conduit for olfactory or tactile information, sending constant pulses of information down to her perfect tiny brain.



The white mutant is historically important. This was the first mutant isolated and studied by Thomas Hunt Morgan in 1910, and its discovery has been described in Jonathan Weiner's *Time*,

Love, Memory (an excellent book, by the way, if you're at all interested in how science is done).

...after all those tens of thousands of more or less identical red-eyed flies, he found a single fly with white eyes.

Morgan's wife, Lilian, who was fascinated by his work and who later (after their children were out of the house and busy in school) made important contributions in the laboratory, was pregnant that year; and long afterward the birth of the new baby became mingled in the family history with the arrival of the mutant. Lilian loved to recall the scene when Morgan walked into her hospital room.

"Well, how is the white-eyed fly?" she asked. According to family lore, he was carrying the fly home at night to sleep in a jar next to their bed.

Morgan told her the fly looked feeble but it was hanging on. "And how is the baby?"

Within a week, one of their two new arrivals was old enough to breed (still another reason to work with flies). Morgan paired the white-eyed fly, which was male, with normal virgin female flies, and together they produced 1,237 young flies. The flies' children (as Morgan called them) had red eyes. The next week, Morgan arranged marriages for all of the children. He was fascinated to see that among the grandchildren, although all of the females had red eyes, about one in two of the males had white eyes. Naturally Morgan thought of Mendel's peas. When Mendel crossed short peas with tall peas, the first generation was all tall, and in the next generation three quarters of the plants were tall and one quarter was short. Shortness in Mendel's pea plants is what is now known as a recessive trait, like blue eyes among human beings. Morgan wondered if white eyes among male fruit flies could be a recessive trait too.

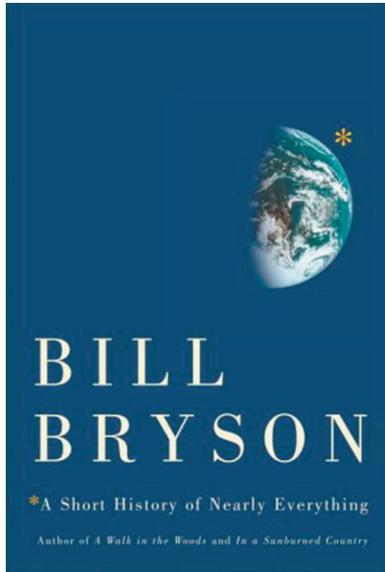
As one latter-day drosophilist likes to say now, "In the beginning there was white." The mutant fly white was the point of entry through which Morgan would establish the modern theory of the gene, the atomic theory of inheritance.



One of the strange things about doing science is that we can look at creatures like this and admire their beauty and appreciate their significance, but of course we also have to be pragmatic. All these pretty little jewels ended up in my fish tanks, where the Danios greatly appreciated their flavor.

WATCHING THE BIRTH OF THE UNIVERSE

BY DAVID SECKO



BOOK REVIEW:

A SHORT HISTORY OF NEARLY EVERYTHING

By Bill Bryson.

544 pp. DoubleDay Canada \$39.95 (Hardcover)

I haven't sat and watched this much television in years. But, it's hard not to when the birth of the universe is on.

And on my television, which gets only one channel with rabbit ears, it's on every night.

So, as Bill Bryson puts it in *A Short History of Nearly Everything*: "The next time you complain that there is nothing on, remember that you can always watch the birth of the universe."

What Bryson is referring to, in such an illuminating and funny way, is that about one percent of the static you see on the television is due to cosmic background radiation, the archaic leftovers of the Big Bang.

Upon reading this, I immediately sat down to watch. I also couldn't help thinking about everything I had learned about...well...everything in Bryson's latest book. Here he has attempted to condense the history of cosmology, physics, chemistry, biology, geology, and much more, into 554 pages. This may seem like an impossible undertaking, but Bryson has done a superb job, entertaining me with clear writing on every page.

Bryson has previously written several well received travel books, including *A Walk in the Woods* and *In a Sunburned Country*.

So how does a travel writer end up explaining the history of many scientific fields?

ELSEWHERE AND OVERHEARD

BY CAITLIN DOWLING

Overheard

“We think it will be particularly beneficial to those who don’t like using a toothbrush.”

Researcher Nikos Soukos on the new light-sabre alternative to a toothbrush, in development in the US. (New Scientist, Ananova.com)

“Should you be smiling while talking about cancer?”

Dr Simon Singh, the Simon Cowell-like judge at *Famelab*, a Pop Idol style contest to get science on television for the masses. (David Adam, Guardianunlimited.co.uk)

“They do look like gremlins, and at first sight it is hard to believe they are real,”

Caroline Brown, senior keeper of small mammals at Bristol Zoo, talking about the Aye-aye, who keepers wanted to call Gollum, after its striking resemblance to the anti-hero of *The Lord of Rings*. (Paul Brown, Guardian unlimited)

“There are two ways of looking at this. The first is that they were doing a ritual dance, but the other possibility is that the man and woman were copulating”

Dr Harald Stauble, part of the archaeological team who appear to have stumbled across one pornography, from the stone age.

“I think that these findings in dogs are directly relevant to the human situation,”

Geoffrey Raisman of the Institute of Neurology at University College London, who is injecting OEG cells (capable of regeneration) into dogs with spinal cord injuries. Many of the paraplegic dogs treated are regaining some feeling. (New Scientist)

Elsewhere

‘Minority Report’ interface created for US military

<http://www.newscientist.com/article.ns?id=dn7271>

Lethal injections called flawed

<http://www.washingtonpost.com/wp-dyn/articles/A54799-2005Apr14.html>

Gut-Level Census Surprises

A report in the online edition of Science shows that almost 400 types of bacteria actually live in the gut...

<http://www.latimes.com/news/nationworld/nation/la-sci-gut16apr16,1,6604544.story?coll=la-headlines-nation&ctrack=1&cset=true>

Making a science out of applied idiocy (say no more)

<http://www.guardian.co.uk/usa/story/0,12271,1461245,00.html>

A SCIENTIFIC EXPERIMENT

BY JAIME J. WEINMAN

Some other people were talking about the silliest things they'd ever done. Their examples beat my own, but then, they'd done more things than I had, silly or no. The one really silly thing I'd done that they hadn't was -- and I swear this is true -- I once tried to see if it was possible to cook all the fat out of a hot dog.

I'm quite serious about this, though, as you can imagine, it happened on a day when I was really, really bored. I had eaten a hot dog for lunch, and I was wondering, how much fat is in these things, how long would it take to get all the fat out, and what would be left? So I took a hot dog, put it in the microwave, and started cooking it. Every so often I would open the microwave, take a paper towel, and wipe off the fat. Then I'd go back to cooking it.

The first thing I discovered was that no matter how much fat had oozed out in the last minute, when you got rid of it, there would always be just as much fat oozing out a minute later. And then another minute later. And still another minute later. In fact, it seemed that no matter how many times I repeated the process, the fat just kept on coming in hot-dog-scale waves. There seemed to be an infinite supply of fat in that little hot dog.

But I persevered. I kept cooking and wiping and cooking and wiping. Then I started soaking the hot dog to wash off any fat that might be trickling back in. This didn't change anything.

Finally, finally, after about ten to twelve minutes of cooking, there was no more fat trickling out of the hot dog, nothing left to cook out of it. And what was left?

A stick. I mean, literally, a stick. It was hard, it was solid, and I could tell that while there was nothing edible remaining, if I repeated the process with another hot dog, I could rub the two of them together and make a fire.

So the result of my silliest experiment on the most boring day of my life was that I discovered what a beef frankfurter is: it is a stick injected with fat. Nothing less, nothing more.

That was the day I gave up eating hot dogs.

CONTRIBUTORS

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Jaime J. Weinman has too much education and not enough food. His writing has appeared in McSweeney's, The Morning News, Yankee Pot Roast, Salon, and his inevitable blog, "Something Old, Nothing New." He lives in Toronto, hot-dog capital of the nation.

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