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## The Future of Information Dissemination

by Roy Auty (G2)

Tired of paying to produce data and then paying page charges to have it published? To add insult to injury, the only way other scientists can read your work is to buy the correct journal! Many have asked themselves why we go through this seemingly silly cycle. The answer is in the question; scientists effectively purchase visibility and recognition, which scientific publishers maintain at a cost. The problem is that the cost is very high: Harvard's Countway library spends one million dollars a year on subscriptions to printed journals and a further \$100,000 on electronic access (<http://www.countway.harvard.edu/ejournals>). As the cost of journal subscriptions continues to increase above the cost of inflation, many libraries are cutting back their subscriptions. This has combined with the increased specialization of most journals to shrink their market to drive up prices and fuel a vicious cycle. So how can this cycle be broken? The publishers have responded by introducing more new titles and charging extra for the convenience of electronic subscriptions, although it is hard to see how this might improve matters. Harold Varmus, soon to step down as director of the NIH, has taken a different approach by threatening to remove the

However, several important questions have not been addressed. For instance, what will happen to journals that are less widely read? This includes many excellent journals that publish material of limited

interest as well as broader interest journals of a lower caliber. If these journals are essential for a field they will survive in one form or another. If not, they will probably not survive and I, for one, will not lose too much sleep over that. Of more importance is the question of Europe. The European Molecular Biology Organisation (EMBO) is upset at being left out of America's plans to have Pubmed Central up and running by the turn of the millennium. The speed of this proposal seems to have been dictated by the need to maintain momentum after Varmus' departure. This sibling rivalry has spawned a new European electronic repository called E-biosci. EMBO claims that their new infrastructure will merely complement Pubmed Central, except that scientists will have to submit to one or the other. This raises the question of whether scientists will ever want to submit their data to

journals altogether.

E-biomed started as a place where scientists could publish articles for all to view, free of charge. Peer-review was an option for those who wanted to appear on the "approved" server. However, it was pointed out that this system favored quantity over quality. In order to restore the peer-review element, E-biomed metamorphosed into a central repository for all articles that had been published by biomedical journals. Sadly, many private journals effectively vetoed this idea by saying they were not prepared to participate. The long term prospects for paper publishing are not rosy and many journals were not prepared to sacrifice their profits. The latest incarnation of E-biomed, now called Pubmed Central, aims to solve this problem by bypassing the journals. Once again, the idea is that authors will contribute to a central repository directly. This can be done instead of publishing in a journal or, with the permission of the journal, some months after paper publication. The system would extend the capabilities of the existing Pubmed to provide the full text of an article as well as its abstract. This proposal appears to offer the best of both worlds. Articles that normally get rejected from the back pages of "The North Luxembourg Journal of Quantitative Molecular and Cellular Biochemical Morphology" will now be happily posted on the web for all to ignore. Papers of a higher quality will still be peer-reviewed for publication in a respectable journal but will become accessible to all eventually.

either of these unreviewed servers. Unless it is recognized as a contribution to science (or a scientist's resume), it probably won't happen. Scientists may prefer being held to ransom by journals rather than risk a worthless publication record.

The problems covered so far are only the obvious ones. The upheaval in publishing will also lead to an upheaval for the libraries. Although it will start as just another website to subscribe to, Pubmed Central may succeed in wiping out the journals and finish by obviating the need for libraries. There will always be a need for libraries that are nice working environments, but they won't be able to compete with a free full-text science library of every journal article. It leaves one with the question of whether libraries should be investing more on journal subscriptions and internet access or comfortable seating. Will the libraries support Pubmed Central as a force to drive down subscription costs or a curse that forces them to close? As the new millennium heralds the opening of a facelifted Countway, it remains to be seen whether the improved seating is up to the job.

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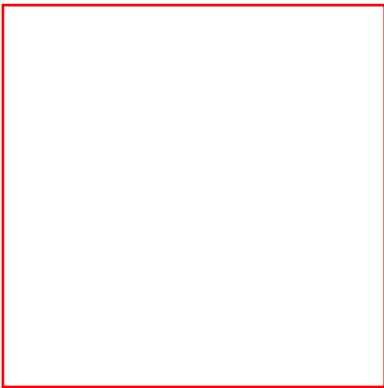
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### Keith Blackwell Assistant Professor of Pathology



**Research Interests:** Transcriptional regulation of genes involved in early cell fate specification in *C. elegans*.

**Beginnings:** Blackwell grew up in Greenville, South Carolina, hometown to Jesse Jackson, Joanne Woodward, and Charles Townes, Nobel laureate and inventor of the laser. He had a strong interest in science, and was also drawn to history, going through a phase where he learned everything he could about ancient Egypt. An inspiring physics and chemistry teacher in high school led him to Duke University, where he majored in Chemistry.

**Graduate School and Beyond:** Blackwell got the M.D. and Ph.D degree, from Columbia University, spending a total of nine years there. The first lab he chose worked on Herpes virus but, after a year there, he realized he was unhappy, and began to question himself and his choice of basic research. Instead of giving up on bench science, Blackwell decided to switch advisors and moved to the lab of Fred Alt (now a BBS faculty member in the Dept. of Genetics), who was about to take his first faculty job at Columbia. There, his Ph.D. thesis investigated antigen receptor rearrangement. He then went back to medical school to complete

his M.D. When he was faced with filling out his match papers to find a residency, Blackwell decided that his real interests were in research, and decided to return to basic science. He did his postdoc with Hal Weintraub at the Fred Hutchinson Cancer Research Institute in Seattle, where he focused on helix loop helix proteins and interactions with specific DNA binding sequences and became interested in nematodes as a developmental system. Currently, Blackwell's lab concentrates on understanding the transcriptional mechanisms which regulate early development in *C. elegans*.

**Favorites:** These include *Absalom, Absalom!* by William Faulkner, the movie "Being There" with Peter Sellers, and spare time doing amateur photography. His ideal holiday would be to go to Egypt, and to see the pyramids, and historical artifacts. Touring Alaska and hiking in the Sierras are also high on his list.

**What single item would he save if his office were on fire?** The first thing that Blackwell thought of was his computer, although he then amended that was pragmatic but not very sentimental. One item of sentimental value that he would take would be a watercolor of an iris that a member of his lab painted for him.

- Soyan Leung

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### Lewis C. Cantley

Professor of Cell Biology Harvard Institute of Medicine



**Research Interests:** The biochemical basis of decision making in cells.

**Beginnings:** Cantley grew up on a small farm in a rural area of West Virginia. As a kid, whenever he asked the question "why," his father would go into detailed and logical explanations about the physical basis of how things happen.

**Graduate School and Beyond:** After majoring in physics at West Virginia Wesleyan College, Cantley found a mentor in Gordon Hammes at Cornell and did his PhD research on the structural mechanism of the F1 fragment of the ATPase. He then joined Guido Guidotti's lab at Harvard as a postdoc, where he studied the mechanism of ion transport across the cell membrane. In both college and graduate school, Cantley's sciences classes were limited exclusively to chemistry, physics and mathematics, and he wonders if he is the only biologist at Harvard who has not taken a single biology class since the 10th grade.

**Favorites:** Cantley enjoys scuba diving and snorkeling in the Caribbean, and lately he has discovered that it is actually more fun without the oxygen tanks. One of his dream holiday spots is

the Cove Castle at Anguilla. The castle is built upon the waters and surrounded by coral reef a place where he can combine scuba diving with gourmet food. At home, he loves reading mystery novels and books on the history of science and philosophy. Other favorites include the Canadian author Robertson Davis and the movie Young Frankenstein.

**What single item would he save if his office were on fire?**

Without much hesitation, Cantley decides to save his computer. In fact he doesn't need the office as long as he has the computer. He spends 98% of his office hours on his computer browsing papers and searching databases. He is able to access his office computer from his home, and he has found an ethernet cable that can reach just about anywhere in his garden. Well, what if one day the Internet were on fire?

- Ji Luo

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### Donald Ingber

Professor of Pathology Children's Hospital



**Research Interests:** How cellular growth is controlled by cell shape.

**Beginnings:** Ingber grew up in the suburbs of Long Island, with an early interest in math. He attended Yale University, where he majored in molecular biophysics and biochemistry. Ingber also took many courses in art

and art history, and was involved in set design for Yale theater. After graduation, he went to England for a summer of research, and then returned to do more research back at Yale.

**Graduate School and Beyond:** Ingber stayed in New Haven, receiving an M.D. and Ph.D. from Yale Medical School. His graduate work on the extracellular matrix and its effects on the cell was done in Jim Jamieson's lab there. It was during this time that Ingber began thinking about how cellular organization could be modeled using the architectural idea of tensegrity, which utilizes a continuous series of tension members in describing a space. He continued with theater and was part of a group which wrote screenplays for situation comedies. Another sideline of those years was drawing canine cartoons for postcards. Because of his interest in clinical work, Ingber struggled with the decision between doing a residency and doing a postdoc, finally settling on

Judah Folkman's lab at Children's Hospital for his postdoctoral training. Among his current activities is an effort to apply accumulating knowledge about organization in natural materials to design and produce better industrial materials and medical devices.

**Favorites:** Ingber and his family spend their free time at their Martha's Vineyard home. He enjoys reading historic scientific literature and the history of science. Favorite books include *Ficciones* by Jorge Luis Borges and *The Crystal Cave* by Mary Stewart.

**What single item would he save if his office were on fire?** He would grab the tensegrity model made by Kenneth Snelson, a gift from the artist himself.

- Karen Fang

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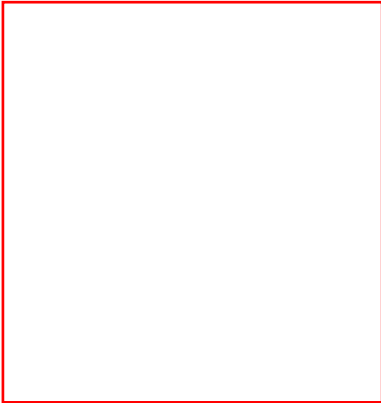
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### Li-Huei Tsai Assistant Professor of Pathology



**Research Interests:** Development of the central nervous system.

**Beginnings:** Tsai grew up in Taipei, Taiwan, where she played violin in concerts and competitions as a child. She went to college at National Chung-Hsing University and majored in veterinary medicine, where she was

active in student government. During college, she dreamed of working in Africa and caring for large animals. But by the time she finished the veterinary program, she did not feel satisfied and wanted to explore more options so she applied to graduate programs in the United States. Tsai started the Masters Program in Veterinary Sciences at the University of Wisconsin at Madison. As a masters student, she took a lot of biochemistry and molecular biology courses through the oncology program at the medical school. The subject matter and inspiring teachers, like Nobel Laureate Howard Temin, made her realize her interest in biochemistry and molecular biology.

**Graduate School and Beyond:** Tsai did her Ph.D. in Virology at the University of Texas Southwestern Medical Center in the lab of Brad Ozanne, where she studied the regulation of Fos and Jun expression in B cell lymphoma. She also purified a novel autocrine

growth factor activity secreted by B cell lymphomas. For her postdoc, she went to Ed Harlow's lab, where she identified several protein kinases, most of which were involved in the cell cycle. She also set up a collaboration with Verne Caviness, a neurobiologist at MGH, to pursue the role of one of those kinases in neural development, leading to her current focus in neurobiology.

**Favorites:** Tsai's favorite pastime is spending time with her daughter. She encourages other women contemplating academic tracks to feel comfortable both pursuing a research career and having children. *One Hundred Years of Solitude* and other books by Garcia Marquez are among Tsai's favorite books because the stories mix fairy tales with reality. Her favorite music is opera. Her favorite movies of all times are "without a doubt, the Star Wars movies."

**What single item would he save if his office were on fire?** She would take her daughter's art with her, since it could not be replaced.

- Laurie Littlepage

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## Genomics and Bioinformatics

by Ji Luo (G2)

As biological science enters a post-genome era, chances are that every other seminar you go to nowadays you would hear people using the words "genomics" and "bioinformatics" in one way or another. Loosely, "genomics" is the sequence and functional analyses of the genome as an integrated system, while "bioinformatics" means the application of computer technology in the management of biological information. In the next two decades, the internet will transform scientific research. Large databases containing the genomic sequences of many species including that of human will be readily accessible, and the ever-growing power of computer programs in making sequence alignments and comparisons, detecting potential coding regions, or predicting protein structures and functions will equip us with the necessary tools to mine valuable information from this vast amount of genomic data. One can immediately see why the two are inseparable: without

pharmaceutical companies and bioinformatics start-ups has presented the search committee with a challenging task: it may take some time before new bio-informatics faculty make their debut in the BBS rotation manual. Several efforts might help attract new talent and secure Harvard's leadership in this field. First, the recruitment should reach a critical mass and enough new faculty positions must be created in the different departments. This would help popularize bioinformatics among the different disciplines. On the other hand, bioinformatics, like "biochemistry" and other interdisciplinary science, should be encouraged as a discipline with its own challenging projects, while keeping the "collaborative" components modest and manageable. Second, the Medical School should continue to improve upon its computer infrastructures. A small cluster of bioinformatics faculty would not suffice: every lab must be conscious of the tremendous utilities bio-informatics has to offer and actively seek out the basic skills to make good use of the resources available. Maybe it is

computers it is impossible to handle the amount of sequence data we amass; and without large amounts of sequence data, any computer-based, genome-wide analysis and modeling would be grossly inaccurate (if not unrealistic).

Harvard is certainly taking these emerging fields seriously and anticipates the future expansion in the disciplines of genomics and bioinformatics. On last count, there are 12 institutes or centers that are set up (or being set up) at Harvard towards the studying of genomics, bioinformatics and proteomics, with a total capital investment of over 100 million dollars. The notable ones are the Lipper Center at the Medical School and the Harvard-wide Center for Genomics Research in Cambridge. Apart from the Lipper Center, which supports research with roots back through one of the earliest grants in the field of genomics and bio-informatics, most other centers or institutes are still in their growth spurt infancies.

Progress has been made at the Medical School in obtaining the technologies necessary for whole-genome studies. DNA arrayers, as well as Affymetrix chip scanners have been running in the Department of Genetics for three years and recently a wide variety of other microarray and proteomic technologies have also been made available at the Medical School. Soon the affiliated hospitals, such as Brigham and Women's, Beth Israel Deaconess, Children's and MGH may have their own DNA chip facilities. So far the existing DNA chip arraying/scanning equipment has been adequate at meeting the demands. In fact, despite the hype of "everybody jumping on the wagon of genomics", only a small number of labs at the Medical School

time for every principal investigator to seriously consider the option of acquiring fast PCs running Linux OS for the lab (they are no more expensive than Macs, and they last a lot longer than a DNA chip). Also, more researchers should make an effort to learn some basic programming and network skills beyond mouse clicking. Third, we should have a clear vision of what kind of bioinformatics projects to pursue at the Medical School. Advantage or necessity may not encourage the pursuit of goals that are in direct competition with the pharmaceutical and the biotech industry. "Harvard worthy" projects must be recognizable as innovative and focused on serving the needs of academic research. Compared to "traditional" approaches, bio-informatics and genomics offer a broader but less in-depth view of a system, thus it is more important to state each challenge precisely with a clear goal.


As for graduate students, it is comforting to know that Harvard has recognized and is working to accommodate the needs for bioinformatics training. Harvard offers bio-informatics courses and training in computer skills. The training program at the Research Computing Center headed by Dr. Bob Freeman at the Medical School is primed and ready for more utilization. Many of us must overcome our reluctance (and fear) of learning computer programming and become comfortable dealing with small-scale code-writing.

Every generation of scientists faces a new horizon because the young are always standing on the shoulders of the passing giants. Great discoveries are often made by those who bravely embrace the new. Genomics is only the beginning; harder yet even more exciting challenges lie ahead. For example, how about the systematic analysis of metabolic pathways, signal transductions,

have so far used DNA chips in addressing their specific scientific problems. One obvious issue concerning many is the cost of the DNA chips, hopefully with healthy competition among suppliers the price will soon come down.

Dr. Phil Leder has been a major proponent of a recent initiative by the Medical School aiming to strengthen the status of bio-informatics research at Harvard. Two new faculty positions specifically on computational bio-informatics have been created at DMS in order to recruit the leading experts in this field. However, good bioinformatics scientists are relatively few, and the fierce competition among universities,

and protein-protein interactions in a cell? The technologies developed for genomics should inspire new approaches appropriate for these purposes, and the tools of bioinformatics would still be tremendously useful. Maybe one day we could really simulate a living cell in the ether of cyberspace. Impossible, you say? But then, who would have thought, back in 1953 when Watson and Crick first proposed the double helix, that they would live to witness the blueprint of the entire human genome?

 Acknowledgement: The author would like to thank Dr. George Church for a very helpful discussion on the topic of genomics and bioinformatics research happening at the Medical School.

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## The Harry Potter Phenomenon

by Dennis Brown (BBS Faculty Member)

Anna Laurilla, 12, of Winchester and her mother arrived at the Barnes and Noble bookstore at 8:00 am on Tuesday, October 12 to wait in line. By late afternoon, the line had swelled to almost 1000, and wound between shelves and aisles in the store, out of the door, and half way round Shoppers World in Framingham. Police backup was called in to maintain order. Free Red Sox tickets? An ice cream giveaway? Howard Stern? A visit by Royalty? Well, close! The event in question was a 7:00 pm book signing by J. K. Rowling, the Scottish author of the sensational Harry Potter series. Allegedly a children's character, Harry Potter, a boy who at the age of 11 discovers that he is in fact a wizard, has captured the imagination of children and adults alike.

After his parents are savagely disposed of by Lord Voldemort (who is so evil that his name must not be said out loud!), Harry (who survived the vicious attack on his family, and becomes

use a "grow your own warts" kit. The magical confections that we are introduced to are hilarious, including "Every Flavored Beans" - pop one into your mouth and hope for the best. The Hogwarts principal, the mighty wizard Dumbledore, tells Harry "I was

*unfortunate in my youth to come across a vomit-flavored one*" and then tries another and chokes "Alas! Ear wax!" Monty Python's influence is felt as cockroach clusters are offered as a treat. The major sport at Hogwart's is

Quidditch, which resembles soccer on broomsticks, and involves catching a winged sphere called a snitch. One-upmanship at this school means possessing the latest model broomstick, a Nimbus 2000 or the fabulous Firebolt. Harry, of course, excels at this game, and a key subplot has his team fighting for the school championship against the mean and cheating bad guys led by Draco Malfoy, a school bully who takes an instant dislike to Harry and does his best to make school life intolerable. And there we have one reason for the success of Harry Potter (all three books in the series have been in the Times best seller list since their release). Harry is supernatural, but has flaws, vulnerabilities and aspirations that remind us of, well, ourselves. We

a hero in the Wizard world) is reluctantly taken in by relatives - the Dursleys - who dote on their own spoiled and repugnant child Dudley, but keep Harry confined to a spider-infested cupboard under the stairs.

All this changes on his 11th birthday, when it is revealed to him that he is a wizard, and he leaves his miserable home to attend Wizard's school, a magnificent Gothic mansion named Hogwarts. This place defies description, but brings to mind Peake's castle of Gormenghast in its size, complexity, labyrinthine dark passages, tunnels and hidden secrets. The school is of course haunted by ghosts, ghouls and poltergeists, some of whom are friendly, some mischievous, and some outright nasty. "Nearly Headless Nick" roams the corridors forever stuck between the worlds of ghosts with intact heads, and those who are members of the elite society of headless ghouls (for which he does not qualify in his present <sup>3</sup>nearly headless<sup>2</sup> condition). Hogwarts is reached by a special train (the Hogwarts Express) that departs from platform 9 3/4 at Kings Cross Station. Of course, this platform is only visible to Wizards (not mere humans, or Muggles as they are referred to by Wizards), and is reached by walking through an apparently solid barrier that separates platforms 9 and 10!

Life at school brings happiness at last, but also danger and adventures with his new Wizard friends, Hermione and Ron, and the hard-drinking, bearded, disheveled giant gamekeeper/handyman/protector, Hagrid, who enjoys reading such classics as *"Dragon Breeding for Pleasure and Profit"*. The wizarding lessons are a joy to attend, as the friends learn to make disappearing potions, cast tickling spells,

sympathize as he is forced to eat bread and water by the Dursleys, we rejoice as he catches the snitch to win a Quidditch game, and we fear for him as he once again has to meet and use powerful spells to fight "he who must not be named", the Dark Lord who killed his beloved parents. Rowlings lets us see our world through Muggle eyes, and through Wizard eyes. She explains mysterious but commonplace Muggle events through the unsuspected influence of Wizards. They like to make car keys invisible (sound familiar?), they have prisons guarded by fearful beings called Dementors, *"something more than air from its surroundings"*. Sometimes, however, the Dementors stray too close to humans (most BBS students have probably experienced the proximity of a Dementor!!). The Harry Potter books will be seven in number - one for each year of Wizard school. In the third book, as he approaches adolescence, he has the first stirrings of attraction to girls, and shows increasing maturity; *"I don't reckon my Dad would've wanted them to become killers just for you"*. The next four books will become progressively darker and more macabre as he moves into the teenage years, but for the moment, Harry has achieved the impossible. He has re-introduced a passion for reading among the difficult 9-13 age bracket, and he is equally popular among both sexes, and among all ages. Three years ago, J. K. Rowlings was an unknown, out of work, single mother. She has now achieved celebrity status - and deservedly so. So I strongly advise you to take a break from your research, read Harry Potter, and discover your inner child!

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*Harry Potter and the Sorcerer's Stone* (ISBN

cause slugs to spill out of an unfortunate  
victim's mouth, control mythical creatures  
and

0-590-35340-3) *Harry Potter and the  
Chamber of Secrets* (ISBN 0-439-06486-4)  
*Harry Potter and The Prisoner of Azkaban*  
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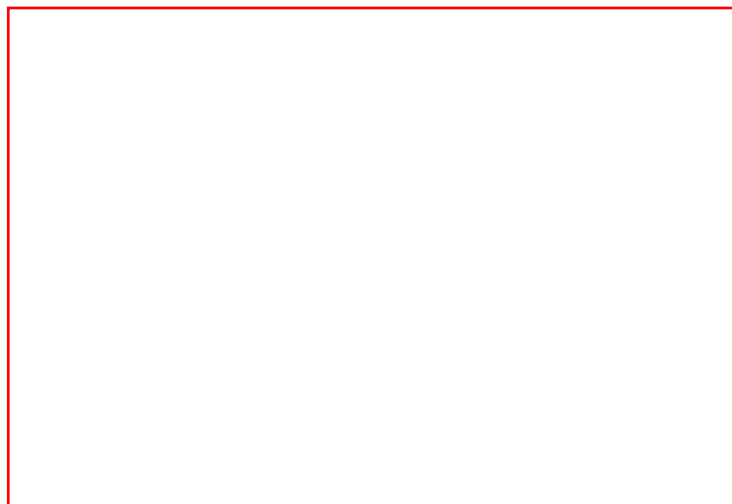
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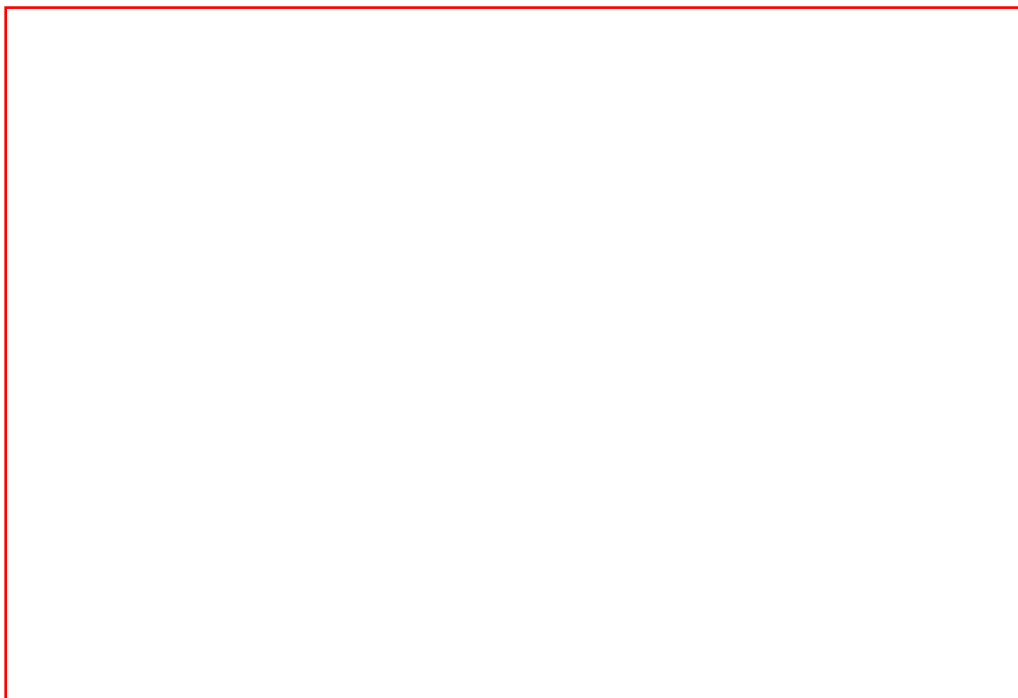
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