Comment

# Still no flying cars

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Published: 27 February 2003

*Genome* ***Biology*** 2003, **4**:106

The electronic version of this article is the complete one and can be found online at http://genomebiology.com/2003/4/3/106



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*Hobbes:* A new decade is coming up.

*Calvin:* Yeah, big deal! Hmph. Where are the flying cars? Where are the moon colonies? Where are the personal robots and the zero gravity boot, uh? You call this a new decade?! You call this the future?? HA! Where are the rocket packs? Where are the disintegration rays? Where are the floating cities?

*Hobbes:* Frankly, I'm not sure people have the brains to manage the technology they've got.

*Calvin:* I mean, look at this! We still have the weather?! Give me a break!

Calvin, the feckless creation of the cartoonist genius Bill Watterson, is a six-year old boy with an overactive imagination, and Hobbes is his constant companion. To everyone else, Hobbes is a stuffed tiger; to Calvin, he appears as a real tiger, with a philosophical bent that matches his namesake. Calvin's complaint, voiced in a comic strip more than ten years ago, was echoed a number of years later by several pundits when the millennium turned. Reporter Cindy Gierhart, in an article entitled "Where are the flying cars?: The future that didn't come true", cited a 1967 *Wall Street Journal* book, *Here Comes Tomorrow!*, that predicted a variety of new technologies for the dawn of the twenty-first century, including trains that moved through air-cushioned tubes at up to 600 miles per hour, a manned Mars landing, and of course, the inevitable flying cars. Yet here we are, in 2003, still commuting to work on outmoded rail systems (misnamed rapid transit), or via 'sport-utility vehicles' so unaerodynamic that they couldn't fly if they had a rocket engine strapped to their rear bumpers.

Futurologists are always being taken to task for their overly optimistic predictions, but the authors of *Here Comes Tomorrow!* didn't do so badly on some counts. One of their predictions was for a worldwide communications system that would transmit vast amounts of information at enormous speeds - this in 1967, when the Internet was not even a gleam in anybody's eye. And they predicted that parents would be able to choose the sex of their child through artificial insemination, although they missed the magnitude of the ethical dilemmas that reproductive technology brought with it. Yet Calvin's complaint lingers. Why, after less than two centuries of almost incomprehensible technological progress - remember that until the mid-nineteenth century no human had ever traveled faster on land than a horse, and no one had ever traveled through the air or under the water at all - has progress in so many areas seemed to slow almost to a halt. We don't travel any faster now than we did in the mid-twentieth century; in fact, if you live in a major metropolitan area, the odds are that most of the time, thanks to traffic, you travel slower than you could have done fifty years ago. After a series of costly failures, we are probably further from sending a manned expedition to Mars than we appeared to be in the late 1960s. We're certainly further from moon colonies: the costs have ballooned beyond expectation. Personal robots exist, but as no more than expensive, largely useless toys. And there are no flying cars. In nearly all the science fiction novels of the mid-twentieth century, and most of the science fiction films, the skies of the twenty-first century were filled with flying cars. Where are the flying cars?

It's actually pretty easy to account for some of the seeming lapses of technological progress. Space exploration became too costly, in men and materials, to justify expeditions that could be done more safely and cheaply by unmanned craft. Public transportation in many developed countries became a poor stepsister to automobiles, although there are signs that this trend, which was driven in part by human laziness and desire for independence and in part by aggressive lobbying by the oil and automotive industries, may be ripe for change. As for the absence of flying cars, well, I think that's the easiest of all to explain. Like all urbanites everywhere in the world I am firmly convinced that my city has the worst drivers on the planet, and if they were given access to flying cars it would be raining automobile parts. I suspect that we have actually had the technology to produce flying cars for twenty years but that it's been suppressed for reasons of public safety, and as a Boston driver all I can say is, it's a good thing.

And yet, for me Calvin's rant resonates in another technology-driven sector, that of publicly funded scientific research. What he was saying, after all, is that he was disappointed that scientific progress hadn't lived up to its promises. He was wrong, of course, because what he was really complaining about was the absence of things largely forecast by science fiction, not science, and science fiction has the habit of making exaggerated promises about the future. But in recent years, biology has also started making big promises about the future in order to justify big increases in public funding, and there are signs that this habit is having serious negative consequences.

It all started, I think, with the War on Cancer, proclaimed by U.S. president Richard Nixon in the early 1970s. I don't think increasing public funding for cancer research was itself a bad idea, but I hated the way it was done (see *Genome Biology* 2001, **2:**comment1007.1-1007.2 for more on this issue). First of all, the title of the campaign conveyed the misleading impression that "cancer" was one disease, and therefore that there should be one cure, a fallacy that the scientific establishment did too little to refute. Second, the whole notion that all we needed to do to solve any major health problem was to throw buckets of money at it ignored the reality that different fields are at very different stages of development, and benefit in very different ways - and sometimes not at all - from injections of funding. Finally, I thought at the time that a cancer war would give the public an overly optimistic idea not only about what publicly supported science could accomplish but also about how rapidly it would accomplish it. Of course, thirty years later, the 'war' has not been won - indeed as described then it never could have been - and no one speaks of it now. Some very important breakthroughs have been made in understanding cancer in general and in treating a small number of cancers, in particular, but perhaps an equally significant outcome was a rise in the number, and influence, of disease activists, who have contributed, among much good, to a proliferation of disease-oriented 'directed' research initiatives, which are slowly siphoning resources from basic, individual-investigator-initiated, curiosity-driven science. And although there is abundant evidence that basic research has significant long-term payoffs, I have never seen an independent study of how effective government-funded applied research is in the biomedical sciences, an issue of particular significance given that at least some of it supports efforts that are amateur versions of the privately-funded research already being carried out by biotechnology and pharmaceutical companies.

I remember the rush of promises made when the gene for cystic fibrosis was identified. More than ten years later, it is not clear that knowing about this gene has contributed significantly to the life expectancy of a single patient. Now I am one of those who believe that some day it will, but history suggests that, unfortunately, some day is probably going to be a long way off. And there were few voices saying that when the gene was discovered. Gene therapy in general is an area where promises of miracles around the corner have been trumpeted. I remember being at a meeting where a respected scientist predicted - his flying cars as it turned out - that by the early years of the present century the drug of choice for most diseases would be a gene, and pharmaceuticals as we knew them would be on the way out. Several patient deaths later, most biotech companies, including several genomics companies, are scrambling to learn how to develop not gene therapies but those outmoded pharmaceuticals. Yet still it seems that every new 'breakthrough' is heralded as taking us to the brink of a cure for this or the way to prevent that.

Genomics hasn't helped counter this trend. The Human Genome Initiative showed that a big, targeted research project could garner huge governmental support, in no small part because it had a well-defined goal that was easy to explain to public officials. And so the effort to sequence the human genome has spawned programs to define the human proteome, and to determine the three-dimensional structures of all of the gene products in various organisms, and several other imitators. The rationale behind some of these initiatives seems to me as thin as the following: if the genome-sequencing people got theirs, then why can't I have mine? Bad enough that data gathering for its own sake - which I in no way condemn *per se*, I merely wish it to be in its proper place - threatens to become more highly valued than hypothesis-driven research. But more dangerous still is the hype that is used to sell such projects to the public and to public officials.

When the US National Institutes of Health was considering starting the Structural Genomics Initiative about five years ago, it convened several meetings to see what members of the scientific community thought about the idea. At one of them a well-known structural biologist stated that in his opinion the project couldn't possibly be oversold. He was old enough to remember the War on Cancer, but evidently he didn't, or didn't think the same risks applied to this project, from which he stood to benefit. And in due course the project was approved, and millions of dollars were poured into a number of consortia that each promised to deliver hundreds of protein crystal structures per year, with the goal of rapidly filling out the catalog of known protein folds and providing functional information via these structures for many of the genes of unknown function that were turning up in the genome-sequencing projects.

The first round of funding for these consortia is now being reviewed, and I suspect that many, if not all, of the consortia are now trying to find other justifications for their efforts. Not one is yet close to the kind of high-throughput that was promised originally. The low-hanging fruit, in terms of protein folds, seem to have been picked pretty thoroughly already, and the number of structures that have to be determined to find a novel fold is increasing, making the completion of the catalog subject to the law of diminishing returns. And the deduction of function from structure is turning out to be about as hard as the deduction of function from sequence, because the coupling between fold and function is not all that tight for many protein folds. I personally think there are sound scientific reasons to fund the Structural Genomics Initiative, but they are very different from those used to 'sell' it. I think a systematic effort to obtain a huge number of protein structures rapidly will lead to big advances in structure-determining technology, will provide an ensemble of structures of great utility for drug design, and will provide valuable information about how protein structure and function change during evolution. Those ought to be reasons enough, but instead the project was, I believe, oversold, and now there is a danger that the funding agencies and their constituencies may lose faith in it.

Much of the process of hyping new initiatives stems from a belief on the part of scientists that the lay public, and their elected officials, do not understand the value of research and need to be persuaded to support it by a steady diet of good news and promises. I think this attitude sells the public short: they're sophisticated enough to appreciate that basic research is a sound long-term investment. After the dotcom bubble, I don't believe that such an investment needs to be camouflaged with exaggerated promises of big short-term returns. "Underpromise but overdeliver", my mother used to tell me. I think that's good advice in many aspects of life, but especially nowadays in science. If we don't want those who support us to sound like Calvin, we'd better either start following that advice, or hope that the general public heeds the title words of a song by the rap group Public Enemy: "Don't Believe the Hype."