Lecture Text

Juan Enriquez: The Life Sciences Revolution: Changing the Language of Business

(*edited for clarity, statistics updated to 2003*)

Business and Oranges

I want you to think about your business in different terms, because I think that you're going to get hit by something similar to what is already hitting biotech and pharma companies. The second thing I want you to do is understand why this thing used to be an orange and why it's becoming something different. And to get there, let's start a little while back.

The Impact of Mapping

In 1492

For all you math jocks, flip the calendar back six months, subtract 500 years, and let's move this class discussion to the Sorbonne, or let's move it to Oxford, or let's move it to the Complutense University in Madrid, all of which were around before this place (Harvard) was.

And if we were having this discussion on the 12th of October, 1492, and we were talking about who was rich and who was poor, what companies were going to be dominant, what regions, what countries, we would have no clue that the world had changed.

And in fact, Columbus landed and didn't know where he landed. First map of the Americas might look a little bit like that. And by the way, we don't know where it is. There's still a debate throughout the Caribbean as to whether Columbus landed on this island or this island or this island. Columbus was not important enough during his lifetime to have a portrait done. Think about that one for a second. All the portraits you see of Columbus are done after he died. Columbus died thinking he landed in the Indies.

The fact that Columbus didn't know where he landed, the fact that the maps look like this, or in fact the maps could have looked like—fast-forward- this a few years later. . The fact that we didn't know what the continents looked like, what the mountains looked like, what the lakes looked like, doesn't mean that the world didn't start changing in an irrevocable, complete way on the 12th of October, 1492. Spain was about to become the world's dominant power; the Americas were about to go through a cataclysm in terms of population, partly because of conquests and partly because of disease, and partly because of slavery. You see the rise and fall of civilizations because somebody started drawing a map.

In 1556

And in fact you go forward a few years to about 1556 and this is the first map of the Western Hemisphere. It doesn't quite look right. There are a few details that are off. The Pacific is smaller than the Atlantic, Japan is in the middle of the Pacific Ocean, and oh by the way India is up above where the Artic Circle is. Again, the fact that the maps were wrong, that they were inaccurate, doesn't mean the world didn't change irrevocably.

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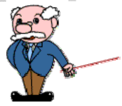

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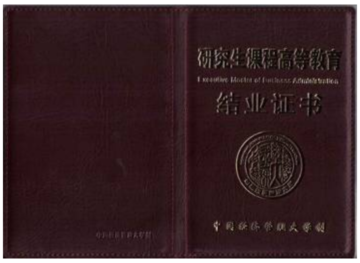

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Nifty stuff. So what?

In 2001

Well, it turns out that on the 12th of February 2001 the single most important map ever drawn by mankind was published on the Internet. Do we know where we've landed? Nope. Do we know where we're going? Nope. Do we have all the mountains, do we have all the rivers, do we have all the continents, have we mapped things accurately? Nope. Doesn't make a difference.

This world has started to change because on the 12th of February we published a map of ourselves, a map of the human genome. And it turns out that you, your best friend, your worst enemy, and a politician differ by about 1 in 1,000 base pairs and that only 3 percent of those base pairs actually code, so the real difference between you and someone in Africa and someone in China, your best friend, your worst enemy, is 1 in 1,000 times 3 percent.

Turns out we're not so different from mice. Turns out we share 95 percent of our genes with mice. That's why when you go into a pharmaceutical company you will see cage after cage of mice, because sometimes, not always, by testing things in mice we can tell what's going to happen in men.

Mice and men are actually quite similar. (Wives know that). In this particular instance, these are mice that have been engineered across the Charles River in Dulac's Lab. And what Dulac did is she took the TRP2 gene out of mice. And normally when you put two male mice into a cage they start to fight and cannibalize each other. If you take the TRP2 gene out, they make love instead of war. They quit fighting.

The Power of Data Transmission

Cave Wall Paintings

So if we are so similar to mice and chimps, what makes us the dominant species on the planet?

This does. The difference between mice and men, the difference between whales and people, or dolphins or higher apes, is this. There are all kinds of arguments and debates and all kinds of nifty research about whether animals learn languages or not. People like Roger Payne, who works at Woods Hole, records songs of the humpback whale, other people work with dolphins, others teach chimps how to sign.

Truth is we don't know. We don't know how good animals are at communicating. But we do know that animals don't do this: animals do not paint cave wall paintings. They can only transmit information if you're within hearing distance or sight, or maybe through urine and smell or touch.

The ability to transmit data in a noncontiguous fashion makes *Homo sapiens* the dominant species on the planet. Because all of the sudden—in this case in Argentina but you can see this in France or Mexico or China—when you paint on a cave wall you're transmitting data across time and you can tell people, this is how you make fire, this is how you hunt, this is what you eat, this is what you don't eat, and the other person doesn't have to be physically present. It's an infinite alphabet and it's non-portable. Can't pick the stuff off the cave wall. But it's the ability to transmit data and to get better at data transmission that powers the economy.

Standardized Cave Wall Paintings

These characters here, hieroglyphs, standardized cave wall paintings. An Egyptian hieroglyph is simply an alphabet that says the following drawings mean the following things. Well it seems pretty trivial. But oh by the way, all of a sudden you can coordinate works in upper Egypt and lower Egypt. You can coordinate works across three generations. You can build really large projects and you can build an empire. Data has become portable, because you put it on papyrus, and it's become standard, people are speaking the same language here and here.

Pictographs and Characters

These Chinese characters do the same thing, they go through the same process. And this built the world's most powerful economy. China has been around and has been powerful for about fourteen dynasties. Twelve of those dynasties have lasted longer than the United States has been a country. This was the dominant power. This power had civil service, this power had the compass, this power had paper, this power had gunpowder, this power had explorers going to the tip of Africa.

How did they start? Well about 3,000 years ago they decided to write "tiger" like this. That's a Chinese pictograph for tiger, and it actually looks like a stick figure of a tiger. And then gradually it evolved into this beautiful stylized calligraphy. That's the contemporary word for tiger 3,000 years later. It goes through about five iterations.

Really powerful method of data transmission. Really powerful civilization. But there's a problem. You need tens of thousands of symbols to transmit data. So imagine a Chinese typewriter before the advent of computers, maybe it reached up to about the second row here.

So what happens to civilization? These folks invented movable type four centuries before the Europeans did. It wasn't Gutenberg who came up with this nifty idea of printing books; it was these folks. Why wasn't it applied? Well, because if you needed to find your way around 10,000 little cubes and then you had upper case and then you had different typefaces, it was really hard to set that type. It was easier just to do it in calligraphy and woodblocks.

What happens to society with this language? You get a Mandarin class. You get a learned class. And not a lot of people down below are part of the knowledge exchange and economy.

If you don't think notation matters—going back to our math jock syndrome—try the following experiment: multiply 11X13 in your head. You can do that. Now try doing it Roman numerals…

Notation matters. The ability to transmit data depends on how efficient you are in your notation system.

Alphabets and Letters

This is how Western Europe becomes dominant. Everything the Chinese said with tens of thousands of symbols, everything the folks in the cave said with an infinite number of drawings, these folks say with twenty-six to twenty-nine letters.

So instead of having 10,000 little symbols to read in your newspaper in the morning, you use twenty-six letters. Really powerful method of data transmission. Then you get Gutenberg, then you print books, then you get people literate, then a whole bunch of people start becoming a part of the knowledge economy, then you start transmitting and exchanging data and technology ever faster… until you invent the machine that is so stupid that it doesn't speak twenty-six letters.

1s and 0s

My little friend over here (computer) doesn't understand ABCs.

My little friend over here understands this. What you're looking at here is the underside of a CD magnified 1,000 times, 3.2 miles, 3.5 miles of spiral code in 1s and 0s. Light/no light. Yes/no.

So what you've got is a language that looks like this. And if I go over to my little computer over here and I punch the number 1, that computer isn't going to read 1, it's going to read the first bit. And if I delete, punch in 10, I'm going to get the second bit. And if I delete, punch in 100, I'm going to get the third bit. And if I delete and punch in 255 I'm going to get this.

If I write something in an e-mail—I'm in a bad mood that morning so I write "I really hate this." That computer is not going to transmit "I really hate this," it's going to transmit "1110001111001". Then I think about it and I say, no, I really didn't mean that, I mean I actually love this. Then what you're really going to do is you're going to manipulate the string of 1s and 0s in a different fashion. You're going to exchange one bit of 1s and 0s for another bit of 1s and 0s.

But there's some really interesting stuff going on in this language because if I were to sing to you—and you don't want me to sing to you—but if I were to sing to you and you wanted to show how off-key I was, what you would have to do is you would have to have a different notation system, because you couldn't do it in twenty-six letters. And if you want to see what I look like, you have to paint a little portrait or you have to take a photograph or you have to do an etching to show what I look like. You can't transmit that in ABC's. But, oh by the way, in this stuff (1s and 0s) you can.

So this little disc right here—don't try this at home kids—when you actually open this thing up… this is what matters, and it's not ABC's. It's little bits. And this little thing right here can hold all my words, written and spoken, can hold music, can hold images. And, in fact, in this particular language you can transmit the contents (printed collection) of the Library of Congress in 1.6 seconds across a single fiber optic line.

You think it's just Biogen and pharmaceutical companies that are being overwhelmed by data? It's happening to all of you, because this language is so powerful at transmitting data that in a reasonable period of time you will have the Library of Congress in your pockets. And if that sounds implausible, one of the things that you should think about is that the Palm Pilots you all use have more computer power than the Apollo 11 lunar landing module. This stuff is happening really fast.

Shifts in Data Transmission and the Global Economy

The Millennial View

Here's what happened to the global economy. This is over a slightly longer period than you look at. This isn't quite quarter to quarter, year to year, this is year 1000 to 2000.

So for the first 1830 years, go to sleep, nothing happened. Wages in Rome in 392 AD were about the same wage as they were in France in 1790. Rules of the game in this economy, well, there was one rule: It was Agriculture. Big country, good thing; a lot of kids, good thing; bigger empire, good thing. Why? Because the way you increased wealth wasn't through individual productivity, the way you increased wealth was by having more kids so they could take care of more goats over more land. Dominant empires on the planet? India and China, 40 percent of the global economy.

And then you had a little shift in the alphabet, you had a little shift in the rules. This little obscure island over in the fog-bound regions, the nether regions of Europe, came up with this nifty idea and they said, "Let's build a machine." Cool, let's build a machine. So they built a little machine. And on this side you've got twelve kids and on this side you've got 1,000 horsepower. Guess who wins?

All of the sudden you get an up-tick in global economic growth. By the way, it's not evenly distributed, because the guy with 1,000 horsepower does a lot better than the guy with twelve kids.

And then you get a knowledge economy. Then you really start getting an order-of-magnitude increase in global economic growth. How does that happen? Well, it turns out that knowledge becomes a really powerful method of creating wealth. We call that a service economy but it's really a knowledge economy.

What's going on in this thing? It turns out that we're getting a huge division between those who understand a shift in alphabet and those who don't.

The Football View

Let's put this in the context of football. We start diverging from apes a hundred yards ago. For the first ninety-nine yards nothing happens. We're hunter-gatherers. Roman Empire happens about seven inches from the goalpost. The Industrial Revolution happens less than an inch from the goalpost, the Digital Revolution takes place about a third of an inch from the goalpost, and the Genomic Revolution is just starting.

The Thirty-Eight-Year View

Here's what happens 1960 to 1998—in thirty-eight years. If you were in the business of agriculture it used to be one-third of the global economy, manufacturing was one-third of the global economy, services and knowledge was one-third of the global economy. Agriculture is now 4 percent. Services and knowledge is now two-thirds.

Watch what happens to Argentina. Argentina says, one peso equals one dollar. That makes a lot of sense. You cut inflation, you control budgets, you have all the kinds of things that economists like, and that works as long as everybody is trading wheat.

But what happens if Argentina doesn't produce knowledge? And what happens as the global economy shifts from agriculture to knowledge? Not because you're producing less wheat or cows or corn, but simply because the relative value of everything else has gotten so big you get irrelevant. The U.S. becomes a knowledge economy and Argentina remains an agriculture economy.

The Price of Commodities

Here's what happens to the price of commodities. The average commodity price is one-fifth of what it was 150 years ago. If you are in oil, if you are in copper, if you are in cows, if you are in wheat, if you are in sheep, you are in big trouble. That's why the wealthy countries of the world today are not oil producers. It is not a paradise to live in Nigeria or Mexico or Saudi Arabia or Iraq or Iran or in the world's former largest oil producer, the Soviet Union. They used to be really powerful nations, but today the richest nation in the world is a small landlocked isolated nation where people make one-third more than the average American does. It's called Luxemburg. There's not a lot of oil.

India and China

Here's what happens to India and China. They go from being 40 percent of the global economy to being 3.4 percent (4.8 percent in 2003). So you've got two billion people, one-third of the globe, producing 3 percent (5 percent in 2003) of the wealth. Not because Indians are different genetically, not because Chinese are different genetically, not because they're not smart. They say that Silicon Valley is powered by ICs. That's not integrated circuits, that's Indians and Chinese. Really smart people, but they choose to work somewhere else, and that has consequences.

ATCG: The New Alphabet

Then these two characters come around. Forty-nine years ago, again in that little obscure island, Britain, Watson and Crick discover a double helix. Think of this as a double spiral staircase. The rungs of that spiral staircase are adenine, thymine, guanine, cytosine—ATCG—and the sides are sugar and phosphate. This is the code of all life. Every life form on this planet is coded in this stuff. If you are a virus, if you are a bacteria, if you are a plant, if you are an animal, if you are a pathogen, if you are a rat, or if you're a man, you are coded in this stuff. It's actually quite a beautiful molecule.

It looks like this when it's crystallized. And a single crystal of DNA looks like this. This is really neat work coming out of Davidson's Florida State University.

If you take the stuff and you run it through a machine… and by the way, as a parenthesis, there are a series of places doing really interesting imaging. There's a wonderful woman at MIT called Felice Frankel. Her next book is about nanotech. We won't get into nanotech much today, but note that there are some images coming out of science that are as good as anything coming out of art.

If you run this DNA through a sequencing machine, you get really boring books. (ATTGGCTTACGTACGTTCCGG…)

This is what the sequencing machines look like, this is Celera, it's a football-field-sized thing. It was one of the largest consumers of electricity in the state of Maryland, it's one of the world's largest private computers, and it's a company that didn't exist three years ago. They are generating knowledge at a reasonable rate. These folks were producing data sets the equivalent to what's deposited in the printed collection of Library of Congress every month, on a compound basis. So take the knowledge set deposited in the Library of Congress. Double that every month on a compound basis with one company.

This is what they write. Not a bestseller. AAATCAGGAAA. If you took your code, code inside one of your cells, and you wrote it out like that, it would be a book about the height of the Washington Monument and it would take you a lifetime to read.

But it's important to be able to read this stuff. Because if you happen to have that particular code in your body, you've got the Ebola, which is one of the deadliest viruses known to man.

Small Changes Make a Big Difference

As you learn to read this stuff, small changes can make a big difference. This is a fruit fly genome—the little nasty things that hang around oranges and bananas and stuff. And this is a particular mutation in position 1,390. And you can clearly see that there's a mistake, there's a T there. Right? You knew that. It actually turns out to be reasonably important for the fruit fly, because what that does is that single letter change means that that function stops, so the rest of this code doesn't get read. Well so what? Well that means that this fruit fly loses all sense of time. This fruit fly has no idea when it should wake up and when it should go to bed. And for a fruit fly that's important, because fruit flies wake up and they have to drink the morning dew, otherwise they dehydrate and die. That's why you won't see that mutation in nature, you'll see it in labs.

You change a different letter, the fruit fly wakes up five hours earlier. Change a different letter, it wakes up five hours later. Is all gene code this simple? Nope. We have just landed right here. We're not even at the map of the Western Hemisphere yet. Just beginning to understand what this stuff does. Change letters in a human being, you get Cystic Fibrosis. Huh. That could make a difference.

Scientists love jargon, so these single-letter changes, they call them single nucleotide polymorphisms. Right, SNPs. So most SNPs don't really matter. Most misspellings don't really matter. But some do. So if you put this in English, single-letter changes or few-letter changes can lead to misspellings, insertions, deletions, repeats, differential expression or mutations: fancy words for stuff you see in the newspaper every day.

If you change a single letter you can change a meaning.

If you insert a word, you can also change a meaning.

And in fact, if you're advertising in Britain and you leave out a letter for a "flat mate"…

You can even take the same string of letters in the same order and just arrange them differently and you'll get an entirely different meaning.

So you can take the same gene code inside the same people, have it read the same, and have two people react in different ways with the same gene code, depending on how the stuff is expressed. That's why when you go to the doctor today, you get a prescription, you go fill it at the pharmacy, the first thing that comes out of that little box isn't medicine, it's about three pages worth of legalese. This stuff should help you, but oh by the way, your hair may fall out, your stomach may fall to pieces, your dog may bite you, etc. They're called side effects.

Why do you have side effects out of the same compound? Why would you take a compound and you take the same compound and nothing happens to *you* but something happens to *you*? Because you can have the same gene code or a slightly different gene code and express it differently and that medicine will have a different effect.

In the measure that we learn how we are different, in the measure that we learn how different molecules dock with different receptors, we're going to start to personalize medicine. We're going to start to understand why some medicines work in some people and they don't work in others, why some medicine go through clinical trials and get through phase three and then crash, because a few people have really nasty reactions to them.

This is leading to the revival of medicines like thalidomide, something that was absolutely *verboten* because of the birth defects. This has all of the sudden become a really important drug because we've learned how to use it for other things. This leads to serendipitous discoveries like you're looking for something for cancer or hepatitis but you find something for MS.

This also has implications for industry structure, because right now it's one size fits all. But if you're in the AIDS drugs business and you're selling Crixovan, well it turns out that now you can tell through little gene chips whether a person is going to react in a different way to a drug. That's exciting because less people get hurt, that's exciting because probably more drugs will come to market. That's also scary for pharmaceuticals because the size of the overall markets becomes smaller.

Mapping Differences With Gene Chips

A company out in California, Affymetrix, takes over a national semiconductor fabrication plant, one of these big fabs that makes computer chips, and what they do is they say instead of putting transistors on these little things (silicon slabs) I'm going to put little tiny hybrid bits of DNA. What those look like is like half of a double helix, so instead of having a full staircase you have half a staircase. And then you take a sample from your blood, or your plasma or something, and you dump it on there, and if something in your blood matches, then this hybridizes, like a zipper. You get the other half, because A always goes with T and C always goes with G. Right? Same sequence, you got that.

Bottom line: this little thingy right here can now test each of you for 60,000 genetic conditions. Pretty soon it will be able to test all the relevant parts of the human genome. It costs 3 billion bucks to get the human genome originally. It cost a private company about 300 million bucks. That same company may sequence your genome this year for about a million bucks, and within five years a lot of you will have your full genome sequenced.

Changes the rules of the game. Because next presidential debate, maybe one of the things I'm going to do is I'm going to come to Charlie, who is running for Congress or for the presidency, and I'll take his glass or his bottle. And you know what? He left some cells on here. So maybe I'll run you through a little gene chip and see what kind of pre-existing conditions you have. Changes the nature of insurance, changes the nature of privacy, changes the nature of medicine, changes the nature of biotech.

Changes how we think about disease, because right now if you go to a doctor, the doctor works on a binary platform. Usually doctors are supposed to say, yes, no, you have the disease, you don't have the disease. Got the disease, do this: Take this prescription, go see this surgeon, do this, do that. Right?

What happens when we start looking at medicine as a series of probabilities? Because what's going to start happening is your gene chips are going to come back and it's going to look something like this.

Leukemia

Now what's this stuff? This is leukemia. Leukemia looks the same under a microscope. Because you know what? It turns out that some people with leukemia go into a hospital and come out, some don't. Why? Some people react well to treatment and some don't. Some people work with one drug and some people work with another drug. Why is that happening? Because when you run leukemia, or what we think of as leukemia, which we thought of as a single disease up to very recently, through a gene chip, then it turns out that you can break out leukemia as ALL, MLL, AML. This is work coming out of the Whitehead Center. Really interesting stuff happening within a mile of here, mile and a half. And what you're seeing here is that in ALL leukemia these genes are over-expressed, these genes are under-expressed. In MLL leukemia, these genes are over-expressed, these are under-expressed. And in AML leukemia, these are over-expressed, these are under-expressed.

So you get a completely different profile for something that looks like the same disease. And if you're an oncologist, you're going to treat these things completely differently, because the prognosis for each of these is different. You're going to be much more aggressive in one instance and you're going to use a conventional treatment in another.

Predicting Disease Probabilities

You can also start to tell what's happening in terms of your probabilities versus the general population. So, for instance, if you're a woman and it comes back that your BRCA1 profile of a specific gene is higher, your chances of getting breast cancer shift right. In other words, you have a higher likelihood of getting cancer at a younger age if you're a woman in a nastier form if you have a BRCA1 or a BRCA2 or a P53. Do you have it? No, you don't have it. Will you get it? Don't know. But your statistical probably is right-shifted.

On the other hand, if you are part of the African-American population it may turn out that you have a higher probability of having something like sickle-cell anemia, which by the way, confers a certain amount of immunity, apparently, against malaria. So there's a tradeoff.

And you can start doing some really interesting archeology with this stuff, because it turns out that AIDS immunity exists among small percentages of the population, particularly white Europeans. You have much less immunity in black Africans. Why is that? Well, it turns out that you can date this specifically, and it turns out that you can date it to 700 years ago. The CCR5 receptor is modified slightly in white Europeans and not in black Africans. Why? Because the CCR5 receptor used to give you a slight edge in survival against the plague. This tremendous population pressure was sweeping across European cities, and those who survived had a slight change in their CCR5 receptor, which also confers today the slightly higher immunity to AIDS. Africa didn't go through the same plague, so you didn't have the same shift.

We're going to start thinking of diseases in a completely different fashion, and your medical charts aren't going to be yes/no, they're going to be higher likelihood of this, take care of this, watch this, maybe that. Much more complex system to run.

Patent Applications

Meanwhile, knowledge grows. Here's what happens at the patent office: The guys at the patent office are minding their own business. They're doing their job. They look out the window, this U-Haul starts pulling out and these guys with white coats and pointy heads start coming out and they've got boxes. Hey, you've got 4,000 patent applications kids. (EST sequences some bundled in a single application)

Four years go by. Doesn't get better. And they've got 22,000 patent applications. One more year goes by and they get hit by 500,000 patent applications for express sequence tags, which are ways of tagging genes.

You can just imagine the scene at the patent office. I mean, boxes are piled up, "Help Wanted" ads are outside, people aren't sleeping, they've cancelled vacations. This blows the U.S. patent system apart and they've got to change the rules on what and how you can patent.

Has it gotten better? Well, it turns out it hasn't. If you go talk to John Doll, who runs the biotech patent area, "John, how's it going?" "It's been a hard week" "Why is that?" "Well you know, I've got this one patent application and I can't get anybody to read it." "Why is that?" "Well it's six and a half million pages long."

Oh by the way, when you get databases that look like that or like this, bunch of things happen. One is this is now the largest source in U.S. patents is no longer IT, it's no longer communications, it's no longer computers. It's bio-related research.

Second thing that happens, you start changing not just the pharma and biotech and insurance industries, you also start changing the computer industry, because these are really big datasets. So all of the sudden you get projects like Blue Gene at IBM.

Changing the Source Code of Life

This funky little thing is called a hydra. It has two heads. They found that because each of your cells contains your entire gene code, there should be ways of programming your gene code so that some cells in your body become something different.

If you go into Cliff Tabin's lab at the Harvard Medical School and you happen to look into a microscope you will go, "Ah!" because you'll see an embryo chicken with many wings. Why would Cliff put together an embryo chicken with many wings? He doesn't even own a restaurant...

But remember when you were kids and you played with lizards, if you picked the lizard up and the tail fell off, the tail re-grew. But if you take a human being, you cut off an arm or a leg, it doesn't re-grow. But what if you can figure out within the gene code that's within your cells how to reprogram that gene code to execute a different function, i.e., how do you take one string of 1s and 0s and substitute it for a different string of 1s and 0s so the function changes? Then you can start thinking about how you're going to re-grow your own skin, your own islet cells if you've got diabetes, the back of your eyes, or your bone marrow.

That's why this thing (orange) is a floppy disk. This is just like this. Take off the outer part and just take the seeds. Seeds are what matters. The seeds are written as AATCAGGACCC.

This little thing is minding its own business in a tree and one fine day it goes kerplunk. And that's the equivalent of taking this thing and saying, ".exe." Execute. Right? So what happens is that little code right there starts going AATCAGGACCC, which means make a root. Next line of code: TACAGGGG, make a stem. Next line of code: CCAGGG, make a leaf, make a flower that's white, make it smell like this, make it come out in the springtime. All that's coded in here. We never read this before last year. First decoded plant, *Arabidopsis,* mustard weed for those who are not into these Latin names, was not published until last year.

That means that if you have the source code and you can read it, you can change the function of this orange, right? That's what this stuff is all about. That's what makes this an exciting area.

This is a baby gaur. I don't think anybody here has seen a gaur. There are a few hundred of these obscure Asian oxen left in the world. Because they're so rare, a Massachusetts company and a conservation group got together and they took a spatula and they scraped some cells out of one of the adult gaur's mouth. Then they took the gene code, floppy disk, out of those cells and inserted it into a fertilized cow's egg and a cow gave birth to a gaur.

So you took the code out of here, changed the code in the cow, and the cow gave birth to a gaur.

They're now experimenting doing this with bongos, elands, pandas, Sumatran tigers. And if you go to Australia, the Australians are fiddling around in their museums with Tasmanian tigers. We don't know how to close the gaps in the DNA yet. But in the measure that we learn how to close gaps in DNA that's deteriorated over time, you're going to be able to take the code of an animal that last walked the earth in 1936 and reprogram it into a wolf and give birth to an extinct creature. This changes the rules of the game.

Here is a Canadian company called Nexia. You're walking through the woods, you're minding your own business, and a spider appears. That spider is hanging from a single thread from a canopy. That means that that is a really powerful material. That's like taking one of you and hanging you by six hairs. Your hair would have to be really strong to be able to hold your weight. The U.S. Army looks at that stuff, says, "Nice stuff, let's get some more."

But you can't have privates milk spiders, doesn't work. You can have privates milk goats. So what you do is you reengineer the genome of a goat in such a way that a goat will produce spider's silk in its milk. That's been done. This is not, you know, "Juan's gone nuts and you're reading science fiction." These are companies that exist.

Why would you want to do that? Because if you're in the U.S. Army, what you're going to end up doing is you're going to end up making uniforms that weigh as much as my shirt and are four times as strong as Kevlar, because if you go in for an operation at Mass General, one of the things you want that surgeon to do is to have an ultra-strong suture material that is biodegradable. This changes the nature of the chemicals business. This is why that little start-up company, Dupont, decides to sell off Conoco for $30 billion and go into life sciences, because the nature of how you produce chemical materials, of material science, is going to change. Because this little orange right here can be engineered to become a vaccine, because Dupont has taken an ear of corn and engineered it in such a way that you can produce a form of polyester that feels like silk that grows in corn.

This is ANDi. ANDi is inserted DNA spelled backwards. ANDi has a fluorescent jellyfish gene inside him, in his cells. Doesn't do anything, unlike Alba the bunny, he does not glow in the dark. But what it means is that you can check whether that gene is getting into every cell. What that means is that you can engineer higher primates. That means that the cloning debate is yesterday. Because the real question isn't, "Do I want a Xerox of myself that's forty years younger?" The real question is, "Do I want to change some things before I make a copy of myself?"

These technologies are going to change the nature of politics, this is going to change the nature of ethics, possibly exploding parties like the Republican party because half of the Republican party thinks that you should be doing this and they're in pharmaceuticals and they're going "yahoo, high tech!" The other half of the Republican party says, "uh-uh, you don't screw around with life and God's word and this, that, and the other." You can get fundamental shifts in politics watching that debate right now in cloning. And that's an old debate. This stuff is moving ahead much faster than that debate.

I don't want to leave you with the impression that this is the only stuff going on that's exciting. It's not just biotech. The reason why life is so exciting and so overwhelming and so full of information and data that a lot of companies are beginning to face difficult and challenging decisions because this is happening across so many fields.

Changing the Rules

We are now beginning to learn how to build things on a billionth of a meter scale. It's called nanotech. And in fact that's happening across the river [at Harvard University]. We had these two characters come across to talk to the Life Science project, and what they're doing is engineering nano wires to sense cancer. This comes out of the *Harvard Gazette*. And what you do is you take a little wire that's built on a billionth of a meter scale and you put some little hybrid probes like those on the end of it and you run current through the wire. And if that current changes, alternates, that means that there's been a hybridization. This changes the rules on what you can build.

I mean, there are people at MIT—again, one of the really exciting things about sitting in Cambridge is all these people start wandering through and it just changes your view of the future, because these guys are thinking on a nano scale of building computers that are as powerful as PCs that float on specks of dust.

But oh yeah, there's another part of the world…

This bio-high-tech stuff is happening in about ten places. It's happening in Cambridge, it's happening on Tory Pines Road in San Diego, it's happening in Silicon Valley, it's happening in Rockville, Maryland, it's happening in certain parts of Britain, maybe some parts of Germany, maybe Singapore, maybe China, but it's not happening in a lot of places.

In fact, it's not even happening in countries, it's happening in specific zip codes. And oh, by the way, this has consequences. Because in an agricultural economy, the difference between what you could produce in a rich country and in a poor country, if you got up earlier, if you had more kids, there's about a five to one differential, putting wheat out, putting corn out.

In a knowledge economy you don't need a lot of people, you don't need a lot of time, you don't need a lot of territory, you don't need a lot of capital to build something that's really big. So the wealth differential between those who are who are educated, who are smart, who are literate in a different alphabet, and those who are not, is now about 427 to 1 and it's headed towards 1000 to 1.

Watch what happens to patents. In 1985 South Korea was producing about the same number of patents as Brazil, Argentina, India, and Mexico. But Latin America never understood the transition to a knowledge economy. They kept producing oranges.

If you don't patent, it's hard to sell knowledge. Of course it's not sufficient to patent, there are a lot of companies that have great patents and don't do well, but if you're not literate and if you don't patent, you are in trouble.

What does the productivity delta look like? Well it turns out it takes about 3,000 Americans to generate one U.S. patent and it takes about 4,000 Japanese and about 6,000 Taiwanese and about 9,000 Germans, 14,000 Frenchmen, 16,000 Brits. Oh yeah, about 800,000

Argentines and about 1,200,000 Mexicans and 1,800,000 Brazilians. Ah ha, and about 10,000,000 Indians and 21,000,000 Indonesians. (2003 figures: 2,854 Americans; 3,636 Japanese; 3,445 Taiwanese; 6,906 Germans; 13,216 Frenchmen; 13,714 Brits; 638,483 Argentines; 1,126,046 Mexicans; and 1,363,248 Brazilians.)

Want to know how India and China went from being 40 percent of the global economy to being 3.4 percent (4.8 percent in 2003)? They didn't get this change, this transition. They didn't understand the new language. Not that they didn't work hard, not that they weren't smart; they simply did not become literate in a new alphabet.

So what happens in Argentina? They say one peso equals one dollar, except that your productivity differential in knowledge terms, which is now two-thirds of the global economy, is 260-fold. That's not sustainable for very long. That's why you can put a guy who is a god of economics, who has got a Ph.D. from Harvard or Yale or MIT or Stanford or whatever in charge of the economics ministry and get support from the World Bank and the IMF and the system is still going to blow apart, because they don't get this transition in language.

Furthermore, you can concentrate or lose this stuff really fast. Smart people want to work with smart people. So IBM last year generated more patents than 139 countries altogether. The margin of error for a government to screw up is getting to be about this big, because in an agricultural economy, if you had a dictator for a hundred years and he was an awful person, your grandchildren would want to go back to take over the land because that land is still worth something in an agricultural economy.

In a manufacturing economy, if you screwed it up for thirty years, the kids wouldn't go back. There are not a lot of you who, if you had a grandfather who had a steel mill in Eastern Europe, would be dreaming about spending most of your life trying to take over that steel mill again. Technology is obsolete. There's probably toxic waste in the place.

In a knowledge economy, you don't need the land; you don't need the manufacturing stuff. Once fifteen 747s leave a country most of the wealth has left the country. You can pick the people that build an economy.

That means that human rights actually really do matter, not just for ethical terms. They matter because people are not subjects, they are shareholders. They can buy a country, they can sell a country, they can short a country. Where those literate brains choose to live is going to determine what's going to power the economy of nation states. It's what's going to make you successful or not. If you don't treat your people right, you're dead.

South Korea, two-thirds of the people who come and get math and science Ph.D.s in this country go home. China, 15 percent. Huge problem for China. It gets really expensive really fast to lose those brains.

Does this have consequences? It turns out that if you'd gone to the United Nations fifty years ago there were fifty flags and now there's 192. Country after country after country is falling apart, splitting, seceding, failing. And you know what? There used to be a reason to take them back over, to restructure, to build an empire, to play Cold War. It's no longer there. In a knowledge economy you don't get most of the value out of oil. United States goes in, saves Kuwait. Say the Kuwaitis had come to the United States and said, "We love you dearly, take our oil. In exchange, make us all citizens, put another star on your flag." No, don't think so.

Different set of rules. Creates a series of really interesting questions for the governments of this planet. This is not just changing pharmaceutical companies but you will find that even consulting companies are beginning to get into this stuff. And you will find that Compaq has the guy who sequenced the human genome on its cover as its poster boy, and you will find that Sun Microsystems is actually beginning to talk about this stuff. And you will find that the energy business is beginning to think about bio-energy conversion ratios. And the food business is starting to think about how they're going to deliver these things instead of through pills. And the cosmetics business is beginning to wonder, gee, could we deliver this stuff through shampoos or transdermal patches or soaps? It's very hard to come up with a business that isn't fundamentally changing.

This is a really interesting set of changes. This is going to change the balance of power of countries, of regions, of companies, and of people. Many of your companies are going to change in fundamental ways because of this new language.

