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Water. New Waters and New Life

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New Waters and New Life

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If this were the Renaissance and you were to pick up a newspaper to see what was being talked about circa the late 1400s, you would find that politicians are corrupt, there is violence in the streets, Muslims are attacking, the government is running a deficit, and either the president isn't very good or the bishop has done something awful. But if you just read the papers you would have missed a very big story, the Renaissance. Newspaper headlines rarely covered da Vinci's finished work or Vasari's architectural drawings changing perspective for all time.

And today you may be missing a very big story simply because the newspapers don't cover it as well as one might want. It is a story about life. The question is "How is life coded and can we recode it?"

There are life codes for stuff that floats around in the oceans and wanders around on land. Each example is an adaptation to its particular environment. Understanding *how* life is coded and *why* life is coded in these ways, and the set of instructions that leads to the difference between two life forms, is an extraordinary adventure.

There are life forms that survive hundreds of times the radiation that would kill you. *Deinococcus radiodurans,* for instance, does the backstroke inside a nuclear reactor. Its chromosomes are blown apart about seven times a day; then they restitch time and again. We now have the full source code, the genome if you will, of this organism. We know how it swims and how it restitches. It is a life form that survives in desiccated format in high radiation environments. And, oh, by the way, space is a high radiation environment. *Deinoccocus'* combinatorial ability will likely soon change molecular biology in a fundamental way.

You can put this particular life form inside really hot ovens and it doesn't kill the prions. They remain contagious on contact. Prions work a little bit like those crystals in the Vonnegut novel of *Ice-9*: when you throw one

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crystal in a liquid the whole solution goes "bing" and becomes crystallized. Because this is a quasi-life form that is not killed by heat or Clorox, or alcohol, it is kind of alive, and it is kind of dead. Prions make proteins fold in a particular way. Because of this, they may be one of the original bridges between the organic and the inorganic.

DNA did not appear in day one. It took a long time to get to cellular life and then to complex life. And even longer for us to even begin to understand its code. We now recognize that all life, as we know it thus far, is structured into long strings of four organic molecules: adenine, thiamine, cytosine, and guanine. So all life is ATCGs. As you begin to study life code you begin to wonder if you could code stuff that doesn't look like DNA. Could you someday transmit life code in more efficient structures and more efficient ways? Or does it have to be based on DNA's four specific base pairs? Could you find life inside methane oceans? Would it be coded the same way?

In the measure that we have the first genome maps, the first full operating code, and we can begin not just to read this stuff but to recode it. The first map of a living organism was published in 1995.[1] By 2001 we had the human genome, the first insect, and the first plant.

Maps lead to discoveries. Some are trivial but fun. You can use the fluorescent markers used by biologists to tag cells and insert them into fish. When you turn off the light, they glow in the dark. Pet shops now sell these animals for about $5, and this is a relatively simple recoding of a life form.

Ameoba dubia may be far more interesting. It has 670 billion base pairs. To put that in context, each human has 3.2 billion base pairs inside of each cell. In other words it is a genome about 200 times as large as that of a human. Because the amoeba only uses a few billion letters to live, it has got a lot of free code that can be used to carry other data. Let me explain further. We can now code anything on binary basis — you can take any of the twenty-six letters that I'm using to transmit this information and code it into binary, which is what this microphone is doing and what that video recorder is doing or what a television or radio does. Which also means you can take the four letters of the DNA code and code them in binary. Say A equals 00, T equals 01, C equals 10 and G equals 11. All of a sudden the digital world and that of biology have become one and the same.

This implies anything you can code in digits — any picture, music or word, written or spoken, in any language — can be coded in a life form or in digital form. Because you've got 670 billion odd base pairs inside this particular life form, the bottom line is, you can store every copy of the *New York Times* ever printed plus its pictures in a few amoebas. And you can clone copies. When you start thinking about computing on a nanoscale, these are really interesting storage structures.

You can also start recoding plants. A Danish company studied the gene pathway that makes leaves turn red in the fall when things get cold and dark. Then the company recoded some weeds in such a way that they would turn red when they were exposed to TNT. So you can spread these seeds and grow green fields. Little red circles appear where there are land mines. The plants are bio-detectors for land mines. You can recode plants for other specific functions including finding pollutants or minerals you wish to mine.

We are not looking at and mapping one organism at a time. Now we are starting to look at whole environments. About two years ago I got on a boat with a small band of buccaneers. The *Sorcerer II* expedition, led by Craig Venter, to ask the question "If we can find a great deal of biodiversity on land, what might be sitting out in the ocean?" Many think of the oceans as a giant Cuisinart. Everything is mixed up more or less evenly with everything else. Is that true? We did not know so ten of us got on a boat and began taking samples of surface water every two hundred miles.

It turns out life has been evolving in the ocean a lot longer than on earth. So, not surprisingly, in retrospect, there is extraordinary diversity everywhere one looks. The first five samples of water of the *Sorcerer II* expedition were taken in what is considered one of the ocean's deserts, the Bermuda Triangle. This area lies between the great ocean currents on the North American and European coasts. There is relatively little wash back and forth within the Sargasso Sea. The area had been characterized and studied by the Bermuda Biological Station for decades. Our expedition took 200 liters of surface water and ran it through three sets of filters.

Then, back in Rockville, MD., using the random shotgun sequencing methods developed by Celera and the Institute for Genomic Research, scientists at the Venter Institute characterized over 1800 new species and increased the number of known genes by an order of magnitude.[2] Environmental genomics is generating some of the largest libraries in the world.

This was interesting enough to prompt us to sail around the world sampling every two hundred miles. We modeled an expedition on the first great circumnavigation for oceanographic research, the *Challenger* expedition (1872–75). Our trip began in Halifax, went across the Bay of Fundy, down the East Coast of the United States, across Yucatan channel, through the Panama Canal, through to the Galapagos. There we retraced some of Darwin's steps and then went across the Pacific to Australia. After the Indian Ocean, and a relatively gentle voyage around the Cape of Good Hope, the boat made its way back to the United States. We kept studying various life forms in a small laboratory we have on board.

I was lucky enough to sail on several long segments of this trip, which occasionally got bouncy. But it is nice being out there. Across the first part of the Pacific we didn't see another boat or a plane or anything else for weeks. Then we reached the Marquesa Islands, which are relatively pristine. Gauguin is buried here. Melville was inspired to write *Typee* and perhaps *Moby Dick*. Thor Heyerdahl's *Kon Tiki* expedition ended up here.

You keep going and it gets even better. You reach the second largest atoll in the world, full of all kinds of friendly creatures like large sharks. All along, where we were allowed to sample by national governments and in international waters, we kept observing life forms that apply very efficient energy conversion. Throughout the oceans, particularly in the areas that have few currents and nutrients, various life forms have gotten very good at taking energy from sunlight. Five samples of water from *Sorcerer II* led to a two order of magnitude increase in the number of solar energy conversion pathways. That will likely have quite some impact on a few businesses.

We also kept looking at carbon-silicon interfaces. These are interesting structures because it is taking carbon code and building their shells on a very small scale. Some of these very small silicon structures actually look like computer chips. There are now many design libraries that can begin to teach us how to build silicon structures using coded life forms. This will likely change the way we build a lot of stuff.

Life sciences are already changing the way we do many things. They are recasting how we think about life, pharmaceuticals, and biologics. And they are having an impact on a very broad set of industrial endeavors ranging from insurance through food, feed, fiber, energy, defense, IT, and cosmetics.[3] If I had a message for young scientists, it is "Start getting literate in this stuff." Most ofthis information is public and free. It is going to change many fields of research as well as power a bio-economy.[4] It would be a good idea for some of you to start on this adventure now.

Notes

1. R. D. Fleischmann, M. D. Adams, O. White, R. A. Clayton, E. F. Kirkness, A. R. Kerlavage, and C. J. Bult et al., (1995) "Whole-genome Random Sequencing and Assembly of Haemophilus Influenzae Rd." *Science* 269, 496–512.
2. J. Craig Venter et al. "Environmental Genome Shotgun Sequencing of the Sargasso Sea" *Science* (2 April 2004): 304. no. 5667, 66–74.
3. Juan Enriquez and Ray Goldberg "Transforming Life, Transforming Business: The Life-Science Revolution," *Harvard Business Review*, March 2000, 96–104.
4. Juan Enriquez, *As The Future Catches You: How Genomics and Other Forces are Changing Your Life, Work, Health, and Wealth.* (New York: Random House, 2000).