Bioinformatics, Nanotechnology & SARS[1]

By

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Who coined the neologism "bioinformatics" in 1987.
Commonly known as the "Father of Bioinformatics"

In the wake of all the news hoopla about SARS (severe acute respiratory syndrome), there were more than enough news, books, merchandize for the average individual to tell apart facts from rumors, science from myth, and reality from hype.

There was a fever for everything SARS: SARS books even though most of the books have nothing to do with SARS except the "new cover design"; health foods to prevent SARS; product to disinfect SARS virus, and use of nanotechnology in SARS prevention or "cure". HAL actually had a visitor from an Asian country who brought a bottle of herbal medicine produced using nanotechnology, with an accompanying book to explain the product.[2]

Drowned in all the information and misinformation overflow, most people, if not all, fail to relate the role information technology (IT), and in particular bioinformatics (BITS), plays in the identification of SARS virus and the various mutants, and a potential cure for SARS. Shut out by news hoopla, even fewer people can look beyond the narrow scope to see the ramifications of the recent SARS outbreak.

Race to Sequence SARS Genome

Patient Zero of the recent SARS rampage is a point of contention. There have been more than enough rumors out there to confuse the average people: some claim SARS to be a bioweapon intentionally released to cause havoc; some claim SARS to be a bioweapon accidentally released from a weapon laboratory; some claim the first SARS patients were in the U.S.… Whatever, the SARS rampage was at one point a public health issue threatening most of the Asian Pacific Rim countries: China, Hong Kong, Vietnam, Singapore, and Taiwan included. Aided by globalization and the ease of air travel today, the disease was reported in many countries, such as Canada, the U.S. and some parts of Europe, with a large number of infections and a significant number of deaths. By May 2003, SARS had spread to 28 countries, infecting more than 7,000 people, and killing more than 500. Of these, China, Hong Kong and Taiwan account for 92.0% of all SARS cases, and 89% of the deaths.

According to one rather reliable source, the first case of SARS occurred in Guangdong Province of China in November 2002. On March 12, 2003, the World Health Organisation (WHO) issued a global alert on the outbreak of the epidemic – a new form of pneumonia-like disease with symptoms that are similar to those of the common flu. This illness is potentially fatal and highly contagious, and had spread quickly to many parts of the world in a matter of a few weeks. In a *tour de force* of genomics, government research centers in Canada and the U.S. decoded the genome of the coronavirus that is all but proven to be the cause of SARS. The British Columbia Cancer Agency (BCCA) in Vancouver was the first to sequence the SARS genome in the early hours of Sunday, April 13, 2003,[3] followed closely by the Center for Disease Control and Prevention (CDC) of the US on April 14, 2003.[4] The discovery's significance will expedite tests to diagnose the disease.[5]

The sequence information in and of itself does not provide a cure. It does, however, provide a test and a diagnostics for this particular virus. The sequencing success was a combination of several events, serendipity being one of the most significant. The challenge was producing a DNA copy of the virus's RNA genome to work with. After several days of effort, scientists managed to produce one millionth of a gram of the genetic material on April 6, 2003. To sequence the SARS genome, the genome was broken in manageable fragments. Within a week, all the fragments had been sequenced. Once started, the sequencing itself was "fairly routine." The sequenced genome fragments were then assembled into the complete genome in mere 12 hours.

The SARS virus genome contains 29,751 bases. The Canadians took considerable pride in narrowly beating the U.S. Centers for Disease Control and Prevention (CDC) in the race to sequence SARS. The CDC announced it had separately sequenced different patient samples of the same virus on April 14. The U.S. sequence contained 24 additional bases compared with the Canadian counterpart.[4]

Role of Information of IT And Bioinformatics

This collaborative effort to sequence the SARS virus demonstrates that the use of genomics crosses the boundaries of health issues. Thanks to IT the expert community could collaborate and work together to expedite the decoding of the SARS genome. Thanks to IT, public awareness has been raised, the average person can read up about SARS, precautionary measures, what to do to avoid infection, and if infected, how to seek help.

In retrospect, the speed with which the SARS genome was sequenced is a combination of two key factors: the high-throughput sequencing machine and bioinformatics. Otherwise, we will still be sequencing the genome. Using the technology of the 1970s, the SARS genome would have taken some three to five years to complete the sequence, not counting assembling the fragment sequences together! But now, with high-throughput sequencing machines, computers and bioinformatics techniques, we can sequence fragments from the complete SARS genome in a few days and use bioinformatics to piece the fragments together to get the complete sequence in twelve hours!

So, bioinformatics, as an interdisciplinary field, is the collection, analysis, management and dissemination of biologically and health-related data. In a more pedagogical definition, it is the study of information content and information flow of biologically-related and healthcare data.[6]

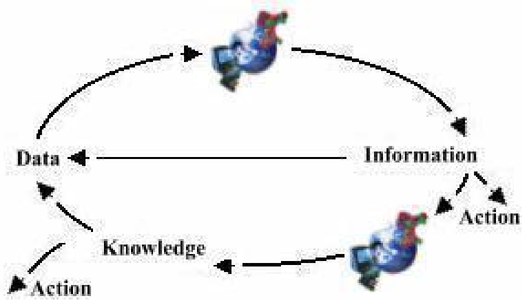

Figure 1. Informatics, when the data used is biologically-related or health-related, it is bioinformatics: Data is input. When data is put in context by human or a computer it becomes information. The information can be put into a storage (computer disk or human brain) as data for further processing, or its relationship with other information can be examined to obtain knowledge. The knowledge can also be put into storage as data for further processing, or it can be used for decision and action. In general, when the dataset is large, a computer can process the data and information much better than a human.

Besides helping in assembling the sequenced fragments into one complete genome; bioinformatics helps in the search in existing virus databases so that scientists know that the SARS virus belongs to the family of coronavirus, which causes pneumonia; bioinformatics helps in the comparison process so that scientists know that the U.S. strain is different from the Canadian strain because the U.S. strain contains 24 additional bases, in fact, we now know that there are more than five mutants of the SARS virus.

Bioinformatics has been a catalyst and turbocharger in helping make drug discovery more cost effective and less time consuming, and in healthcare. It will continue to play the important role in finding a cure for SARS. In fact, there are claims that a cure for SARS could be found in 5-6 years! Such claims would have been ludicrous if not because technology has advanced to a much more efficient state and that we are more proficient with bioinformatics.[7]

Nanotechnology

Nanotechnology is expected to thoroughly affect the way science addresses medicine, food, electronics and the environment. By 2015, the yearly market for products that carry nano-components, including all computer chips, half of pharmaceuticals and half of chemical catalysts, will reach $1 trillion.[8]

By way of comparison, the current state of nanotechnology mirrors the level of development in the field of polymers and plastics in the 1930s. In the 1930s, the polymer and plastic industry was still in its infancy. The industry quickly grew, providing the materials for a large portion of manufactured goods. Nanotechnology industry is currently in its infancy, but several basic breakthroughs have been made.[7,8]

In particular research and development of nanotechnology pertinent to our discussion, there have been various claims, many opportunistic, but a few are reliable. To exacerbate the confusion, SARS came at a time when the U.S. and U.K. were declaring a war against bioterrorism. Businesspeople see this a great opportunity to request for more funding or to seek expedite approval from government agencies.

In general, all of these technologies involve a top-down approach of nanotechnology, that is, start with macroscopic sizes to get something in supertiny sizes. For example, grinding titanium dioxide (TiO_2) to nano-fine powder. (The other approach – bottom up is what most people are familiar with when we talk about nanotechnology: position atoms exactly where we want them to create new materials).

Akira Fujishima and Kenichi Honda discovered photocatalysis in 1972, thus setting off a photocatalysis industry.[9] Mediums for photocatalyst are numerous: TiO_2, ZnO, SnO_2, CdS, ZnS… Among them, TiO_2 has the most desirable properties and it has become the ideal candidate. Naturally, TiO_2 exists in three states: anatase, rutile and brookite, but only the anatase state has the ability to absorb light. (The rutile state is stable at high temperature and is an ideal candidate for use as a sunscreen). Photocatalyst TiO_2 can be used in the decomposition of NO_x, the exhaust gas from automobile; in the removal of foul odor from acetaldehyde, anemone, trimethylamin, hydrogen-sulfides, methyl-melcaptan; in the prevention of dirt building in living environment; in treatment of water to remove dissolved organic compounds, chlorine, and other pollutants; as bacterial disinfectant; and as sunscreen.

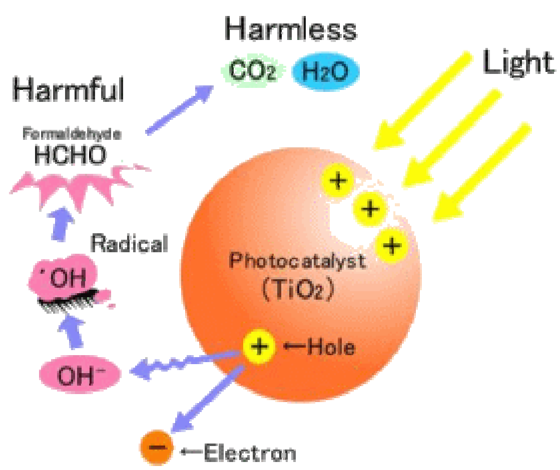

Figure 2. The figure shows how photocatalysis works, in this particular case, as a disinfectant. When the surface of the TiO_2 transparent thin film is exposed to UV light (~400nm), negatively charged electrons are released, in much the same way as electrons are released when sunlight hits the surface of the silicon solar power cells. Simultaneously, positively charged holes are formed on the surface of the thin film.

Under UV light, electron-hole pairs are created. The negative electrons and positive holes create very strong oxidizers, called hydroxide radical, even stronger than chlorine used as a sterilizer. When harmful substances stick to the positive holes, they are completely broken down into the carbon dioxide and other harmless compounds. As a disinfectant, the hydroxide radical also can inhibit the growth of bacteria and mold.[10]

Bacteria are all over the place and they multiply fast. Within an hour after conventionally disinfecting using bleach for example, the disinfected body will have returned to 80% of pre-disinfection state; and in further 23 hours, it will have returned to the original state. The idea is to have a disinfectant agent, such as TiO_2 that will kill bacteria faster than they multiply to sustain cleanliness.

For TiO_2 to be effective as a disinfectant, the size has to be in the nanometer (10^{-9} m) ranges. In this size range, it has been shown scientifically that TiO_2 can really disinfect bacteria. The effective can go as high as 70%-99.9%. But as a disinfectant for viruses, particularly for SARS virus that can last up to three hours outside the patient's body, scientific evidence is still pending.

But the cost to grind the substance increases with diminishing size. Many businesspeople now use micrometer (10^{-6} m) range TiO_2. Though much cheaper, the effect is drastically reduced.

On May 23, 2003 and during the SARS epidemic, the WHO recommended that the cabin or quarters occupied by a SARS patient be disinfected with sodium hypochlorite bleach and formatin 1 or chloro meta xylenol. There have been technologies developed along this line to deliver one of these ingredients at an extremely low concentration to create a powerful hospital grade disinfectant that is non-hazardous and environmentally safe. One particular product line, employing unique nano-emulsive technology, is reported to be able to reduce the spread of a broad range of diseases, including E. coli, salmonella, listeria, staph, strep, pseudomonas, MRSA, VRE, Norwalk-like virus, Influenza A, Hepatitis B and C, vaccina…[11]

Another product has been developed using proprietary technology to create a nano-emulsion. The nano-emulsion can be sprayed, smeared on clothing, vehicles, people or anything that has been exposed to a slew of deadly substances. It can also be rubbed on the skin, eaten or put into beverages like orange juice, and used in the water of a hot tub. The working principle is the nano bubbles contain energy that is stored as surface tension. The energy is released when bubbles coalesce, thus zapping the contaminant. The hurdle is that a huge amount of energy goes into making the nano-emulsion, bubbles of size smaller than the bacteria and viruses.[12]

Such and other claims are quite reliable; many other claims are groundless. For those products which have been scientifically proven feasible, for them to get into the market, the cost for producing them will have to come down drastically so that they are affordable.

The major concern is that opportunistic businesspeople seize the opportunity of SARS fear hysteria to market affordable prevention kits, disinfectant substances, sterilizing systems… at the expense of the effectiveness of the kits, substance or systems. In such scenario, the public may lower their guard under the false impression that they are fully protected.

Malaysia is also active in these areas. Current ongoing efforts include the nanobiotechnology effort, headed by Professor Datin Khatijah Yusoff at Universiti Putra Malaysia, and NanoBiotech Sdn. Bhd. (425296-M) at UPM-MTDC Technology Centre. The main focus is to use nanotechnology as a means for detecting infectious agents, or to develop diagnostic platforms. Professor Nor Muhammad Mahadi and Professor Rahmah Mohamed of the National Institute for Genomics and Molecular Biology, one of the three institutes of BioValley, are leading an effort to sequence the SARS genome.

Note that all the products, if they are effective, are good only for preventing, disinfecting or detecting infectious agents; they do not offer a cure.

The SARS Lesson

SARS still has no known cure at present. It may be spread directly by inhaling the microscopic, airborne droplets left in the air by a SARS patient. Alternatively, the virus can survive up to several hours outside the body and touching an object that has become contaminated when coughed on, sneezed on, or touched by a SARS patient may spread infection.

The fact is that each year during the flu season, the flu hits 95 million Americans and kill some 20,000 annually; the leading scourge and a preventable man-made plague – smoking kills about 3 million worldwide each year from smoking-related illnesses;[13] of these 10,000 are Malaysians.[14] By comparison, SARS infected less than 10,000 people, killed less than 1,000 victims, and yet the public response seemed to be much more immense. The response to the outbreak of SARS in Asia is a typical example of mass hysteria. Knowing that there is still no cure for SARS, the public responded with an epidemic of vulnerability, an outbreak of mass psychogenic or sociogenic illness.[15]

The good news is that the rampage of SARS has ebbed for now. The bad news is SARS will likely return in the future, and just like SARS, other emerging diseases unbeknown for now, will surface in the future.

SARS and emerging diseases have become a global issue for which every responsible citizen has a duty to help his or her government to contain. There is no doubt that our genetics plays a huge role – certain people are more susceptible to disease attacks, while others are not, technology and public awareness can only play a significant ancillary role. The best measure is still environmental sanitation, personal hygiene and physical fitness. Prevention is better than cure. Make it a point to take good care of your health.

References

1. Parts of this article are based on live interviews in Los Angel, San Francisco, and Taipei.

2. HAL is the name of the supercomputer HAL9000 in Odyssey 2001. HAL are also the initials of the author.
3. Marco A. Marra, et al, “The genome sequence of the SARS-associated coronavirus”, *Science*, May 1, 2003.
4. P.A. rota, et al, “Characterization of a novel coronavirus associated with severe acute respiratory syndrome”, *Science*, May 1, 2003.
5. John Dodge, “Decoding SARS virus breaks new ground in genomics”, *Bio-IT News*, April 15, 2003.
6. Audrey Edwards, “Proud Pioneer of Bioinformatics”, *The Star*, June 15, 2003
7. Hwa A. Lim, *GENETICALLY YOURS: Bioinforming, biopharming, and biofarming*, (World Scientific Publishing, Inc., 2002), 418 pages.
8. “Cleaner living through nanotech”, *Associated Press*, September 9, 2002.
9. Akira Fujishima and Kenichi Honda, “Electrochemical photolysis of water at a semiconductor electrode”,*Nature* 238, p.37 (1972).
10. See for example, the website of Photo-Catalytic Materials, Inc.
11. “Nanotechnology cleaner/disinfectant effective against SARS”, *Infection Control Today*, June 9, 2003.
12. Heather Newman, “A nanotech company that’s so clean, you can eat of it”, *Small Times*, December 13, 2002.
13. “Tobacco death toll”, *Human Resource Development and Operations Policy*, World Bank, February 1, 2003.
14. “Chua: 10,000 deaths linked to smoking”, *The Star*, August 27, 2001.
15. M.D. Feldman and J.M. Feldman, *Stranger Than Fiction: When our minds betray us*, (American Psychiatric Press, Inc. Washington, DC, 1998).