personal digital cyberarian regularly assures me that my own branch densities are as respectable as those of my elderly peers.

So science has survived and thrived. It is different now. Its practitioners are different. It is cheaper, faster, and more open to more people. It has become a dynamic enterprise linking the physical world, the virtual world, and the world of human imagination in ways that were only dimly perceived at the end of the last century.

Now at midcentury, we are faced with the rise of powerful artificial intelligence systems. These systems not only make possible much of our speculative scientific work, but some are beginning to formulate hypotheses of their own. The next 50 years for science and for the AAAS are likely to be spent making room within *in silico* research for *in silico* researchers. I happily leave that emotional and evolutionary challenge to you.

Thank you and good afternoon.

The author, a Maryland-based microbiologist who has abandoned the lab for the Internet, wonders whether H. G. Wells was right in asserting that "we are inclined to underestimate the certainties of the future." E. McSweegan, 1692 Barrister Court, Crofton, MD 21114-2602, USA. E-mail: edwardmc@qis.net

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Traditional and Cybernetic Sciences Combine to Combat Human Viruses

by CAURNEL MORGAN

Two researchers from different laboratories, with different scientific approaches, and from different eras are trying to demonstrate the strength of diversity in combating human disease.

Robert Jackson is a 108-year-old scientist with an M.D. in psychiatry and a Ph.D. in virology from the American Mental Health Research Institute (AMHRI). Dara Olu, of the American Biological Research Institute (ABRI), is a 23-year-old who has earned a Ph.D. in the emerging field of pixel biology from the ABRI, with an area of specialization in pixel genomics. She also has degrees in business and politics. Whereas Jackson runs a traditional brick-and-mortar laboratory at the AMHRI, Olu directs her independent laboratory in cyberspace. Together, Drs. Jackson and Olu head a team of scientists that is applying a novel approach to the treatment of viral infections.

A number of viruses have been successful in attacking humans because of their capacity for rapid mutation. The eradication of viruses that caused certain cancers, acquired immunodeficiency syndrome (AIDS), and other diseases were complicated by the viruses' ability to mutate in a relatively brief period of time after infecting humans. In the 20th century, the standard approach to studying human viruses was to isolate a viral culprit after an epidemic had occurred. When this approach was used, some viruses were well on the way to their second or third generation of mutations before effective therapeutics could be designed. However, the fight against viral infections was dramatically altered from the last decade of the 20th century into the first two decades of the 21st century. During this period, a number of DNA analogs with nonphosphodiester backbones were developed. These various forms of engineered nucleic acid (ENA) were used very effectively as antiviral agents (Jackson 2013).

Dr. Jackson pioneered the use of ENA antiviral technology. A number of DNA derivatives were designed in which the phosphodiester linkage has been replaced but the deoxyribose retained. However, only a few of these appear to be good structural DNA mimics. The first two successful attempts to replace the entire deoxyribose phosphate backbone resulted in morpholino derivatives and the polyamide nucleic acid (PNA), which contains a pseudopeptide backbone (for review, see Jackson 2007). These designs determined that the deoxyribose backbone is not essential for DNA mimics. ENAs have been demonstrated to form double and triple helices with themselves and natural nucleic acids (that is, DNA and RNA). The antiviral property lies in the ability of the ENA to bind to viral nucleic acid in a sequence-specific manner. This approach permitted Jackson and other virologists to target mutant forms of viruses as soon as their nucleic acid sequences could be determined (Jackson 2009).

Today, a large variety of engineered nucleic acid (ENA) is used to form sequence-specific double and triple helices with viral nucleic acid. Once formed, these complexes can halt the ability of the viral genes to serve as templates that direct the host cells to make viral proteins. One obstacle to applying ENA as an antiviral agent in vivo is that ENA entry into host cells typically occurs at a slow rate under normal conditions. However, the inclusion of a nuclear localization sequence (NLS) can dramatically increase the rate of sequence-specific ENA entry into cell nuclei. NLS-mediated ENA uptake occurs several times more efficiently than with ENA alone. Additionally, destruction of the

infecting virus can be effected by the conjugation of the ENA to an antigen for a known antibody. Thus, when the antibody is injected, it binds the ENA–viral RNA complex. These findings were instrumental in establishing ENA technology as an antiviral agent.

With the advent of pixel biology in the second decade of the 21st century, scientists were able to model human viruses and to design highly specific antiviral ENA probes, based on the viral characteristics and viral-human genomic interactions. The emerging field of pixel biology, pioneered by Olu, uses artificial intelligence modeling (AIMing) to simulate the characteristics of a virus within a host environment. The pixel biologists then model the effects of therapeutic agents, such as antiviral ENA, on viruses. Although this technology is still in its infancy, it has resulted in the destruction of a number of lethal viruses.

After the eradication of viruses that contributed to major human diseases, scientists turned their attention to the study of viruses that have been recently discovered to cause nonlethal alterations in human behavior and physiology. One such virus is the humor deficiency virus (HDV), which depletes the sense of humor in a relative small population of adults, many of whom become politicians (Adams and Luperena 2050). HDV is the first virus reported to attack the neural substrates for humor, and its control signifies an important step in combating other neuron-attacking viruses that may have more detrimental consequences. The HDV nucleic acid sequence has 99% homology with a portion of the recently cloned human humorostatin (hHst) gene, which is overexpressed in some humans (Rushon *et al.* 2048). HDV is now known to inactivate the joy kinase/signal transduction and termination (JOKE/STAT) signaling pathway (Adams and Luperena 2050).

Recently, the research team, led by Jackson and Olu, reported the *in techno* destruction of the HDV (Jackson and Olu 2050). The AIMing approach, says Olu, "is an effective model for targeting viruses that is demonstrated to be more than 85% accurate." So, although the stage is set for the *in vivo* eradication of a newly discovered human virus, the real work is yet to begin. The scientists have completed the first step of the process for testing experimental therapeutics. They have completed the *in techno* effects of the therapeutic agent using AIMing. The two remaining steps include *in vivo* modeling and clinical trials. By invoking the *momentum continuum* principle, these scientists who reported the results of this AIMing study are permitted 6 months to follow up with *in vivo* modeling, and 2 years to complete their testing with clinical trials, before others can weigh in at each step. Jackson says that "the *in vivo* modeling has already begun and the preliminary results look promising." HDV antireplication ENA has been produced with a renal localization sequence (RLS) and conjugated to visible red protein (VRP) tag (Olu 2050; Olu *et al.* 2050). The bond between the HDV-antireplication ENA and the VRP-RLS tag is slightly less stable than the bonds in ENA. At a time before the ENA ceases to exert its biological activity, the tag dissociates and is excreted via the urine. As more of the tag is concentrated in the urine, the color changes from orange to bright red, thus providing a convenient way to chart the decay of the ENA.

Jackson and Olu anticipate that clinical trials will begin in several weeks and hope to report their findings in a year or so. However, they are both reluctant to discuss a setback that occurred at the *in techno* level in the Olu cyberlab. A cyberanimal rights activist group, called People for the Ethical Treatment of Artificial Genomes (PETAG) hacked into the Olu laboratory data computers and "freed" some of the human-viral genome models. Although the work was reproduced from backup data, the project was set back an entire day. Dr. Olu would only say that pixel biology is necessary to decrease the use of "real animals." Dr. Jackson remarked that he had not seen this kind of reaction since the animal rights sit-ins of the twenties. "I mean the 2020s, I haven't been around that long," he quickly added. Both Jackson and Olu are confident that future experiments will proceed as planned, and both are looking forward to many years of collaborative work together.

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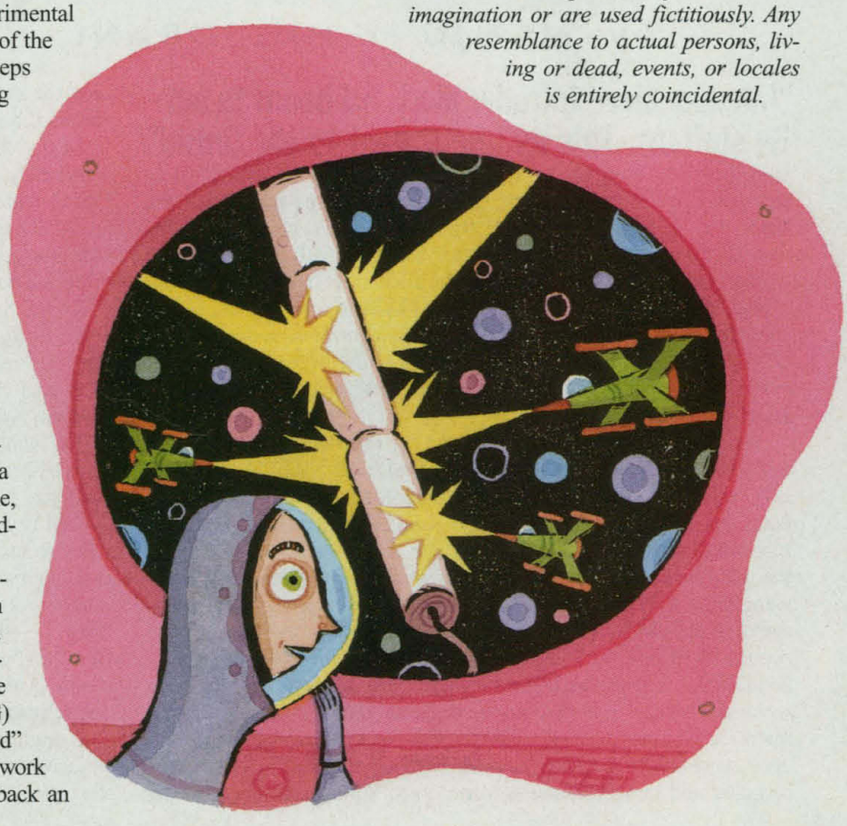

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