BINF sights.

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Bioinformatics in Defence

how computationally modelling genomes can help fight against weapons of mass destruction

P04 FEATURED ARTICLE
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BIOLOGICAL WARFARE:
THE NEW FRONTIER IN EMERGING GLOBAL THREATS, AND HOW COMPUTATIONAL METHODS CAN COMBAT THEM

[ONGOING RESEARCH PROJECTS]

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To every man is given the key to the gates of heaven. The same key opens the gates of hell. And so it is with science.

— Richard Feynman

antivirus software for weapons of mass destruction

Bioinformatics often resembles data science, used in applications for disease prevention, medicine, pharmacology and supporting further research into biological systems. But bioinformatics has also seen use in one particular area that many may be unaware of: defence and national security.

Writer *Cam McMenamie*

Bioinformatics in Defence

Throughout history, advances in technology have shown many benefits and positive changes to society. But each advance in technology also comes with the ability to be misused. Perhaps the most extreme example of this is the pursuit of biological knowledge, in which vast quantities of data on disease states and pathogens have allowed the treatment of many diseases; whereas this new knowledge has also been used in the development and proliferation of biological weapons. With new knowledge of how cells respond to viral or bacterial attacks, new cures could be made: but with that same knowledge, others may seek to find ways around the cell's defences and make strains of viruses more deadly than what mother nature had previously allowed.

Whilst the wielding of this sort of technological power has often been thought of as belonging to governments and nations; advances in the biotech field in recent times allow the restriction of the individual to rapidly shrink when it comes to this kind of capability.

Some of these technologies that are becoming visible on the horizon already have governments and security agencies worried. For example, a DNA printer that generates any piece of biological code is already here. CRISPR gene editing kits can be purchased for a few hundred dollars and used in a garage DIY laboratory. The complete sequenced genome of a deadly strain of anthrax can be found with a simple BLAST search.

The line between the organic and synthetic is being blurred.

For a roughly analogous scenario, one can look at the emergence of home computing in the 80s and 90s. As digital technology became increasingly available, communities of hackers and cybercriminals appeared to develop computer viruses and sophisticated ways of getting through online security measures. One individual with a laptop could wreak havoc that a few decades before, would have required the full effort and funding from an entire country. In a similar way, a new advent of digital technology is emerging - only this time, the viruses need not be restricted to cyberspace. The barriers previously existent between the physical and virtual are collapsing. The line between the organic and synthetic is being blurred.

One can only imagine how these biological tools may be repurposed in the near future for malicious purposes -- and the truly devastating potential they may have. We only need to look at the current pandemic situation to show us the sheer weight that a public health crisis would have on the world -- and the effectiveness of the world's response, or lack-thereof. The potential to produce real, malicious biological effects may seem like sci-fi to some, but the increasing ability for lone individuals or non-state actors to affect the world in previously unthinkable ways has many institutions and government bodies alarmed.

What is being done to stop these threats?

Next Gen Sequencing

The Australian Department of Defence has funded several research activities over the past few decades into genomic sequencing and disease modelling. In particular, Next Generation Sequencing (NGS) technology has been a key focal point. DoD has a keen interest in NGS for detecting, identifying and characterising viruses and bacteria; forensic genotyping; and measuring RNA responses to chemical and biological factors.

One example of this is the research efforts into Ricin, a cytotoxic protein produced by the castor oil plant (Ricinus communis). Ricin was notably used in the assassination of Georgi Markov, a Bulgarian journalist. In London, 1978, Markov was shot and poisoned by a Ricin-containing platinum-iridium pellet. While Ricin has been known for its potential in small-scale criminal activity, a more worrying thought is that it may be used on a mass-scale basis by a non-state actor, rogue government, or terrorist group. The castor oil plant from which the poison is derived is available around the world, and grows rapidly. A simple DIY extraction of ricin from the plant is fairly easy (many of the instructions could be found online), but the refinement process leaves behind 'DNA signatures'. The Australian Defence Intelligence Community aims to exploit this fact by developing well-characterised maps of castor bean seeds and their DNA, allowing a ricin source of interest to be traced back to how it was made. Linking various strains together can help paint a picture that may identify, and thus control, where ricin is being sourced. In order to do this, the research project aims to find genetic 'markers' in Ricinus communis that can be used in later forensic investigations. These could be identified through computational methods, once a large set of short-read sequences are made from a database of castor bean seeds.

This would help confirm toxic preparation of specific plant material; assign plant material to their nearest genotypic cluster; and, importantly, infer the geographic origins of the plant material of interest. For example, one sample of plant material under investigation in Australia may be traced back to another continent, and even a specific region.

Biological Defence

Defence also comprises a Biosurveillance and Biodetection group, which leads research and development into microbiology and informatics to produce **biosurveillance** and **health monitoring** capabilities. This is essentially the ability to detect, identify and assess biological dangers from natural sources, or potential adversaries (ideally well before they become an imminent threat). The fields involved in biosurveillance include microbiology, immunology, biochemistry, analytical chemistry, mathematics and statistics.

DARPA

In the United States, the Defense Advanced Research Projects Agency (DARPA) is currently undertaking an initiative to rapidly and accurately screen individuals for exposure to Weapons of Mass Destruction (WMDs). Under the Epigenetic CHaracterization and Observation (ECHO) program, this project aims to develop a portable device that can read the epigenomic 'signature' of a human by obtaining a simple fluid sample (a drop of blood, or a nasal swab) to observe their detailed history of exposure to various chemical or biological agents.

Whilst an individual's genome (the one-dimensional DNA letter code) remains constant throughout their lifespan, their epigenome (the way their genes are expressed) can be changed in response to varying environments. Changes in structure of the DNA strand and proteins called histones allow certain sections of the DNA molecule to be 'open' for transcription to RNA, and thus the expression of genes in various ways can be regulated without a single change to the actual genome itself. Exposure to pathogens or hazardous materials (such as those implicated in WMD development) may leave a 'fingerprint' in the individual's epigenome, and when analysed, could mean the difference between life and death.

The project first requires the development of a portable sequencer that can rapidly analyse epigenomes at the molecular level, and perform onboard diagnostics. The bioinformatics performed by the device must be based on some paradigm of epigenomic 'signatures', and this requires procurement of a training dataset of pre- and post-exposure epigenetic measurements.

To develop the training data and test that the system indeed works, samples of patients with Methicillin-resistant Staphylococcus aureus (MRSA) infections taken over 20 years will help identify the specific 'signatures' of certain biological exposures. Additionally, results can be used from an unrelated study on the effects of organophosphate exposure to farmworkers. Organophosphates are used in insecticides for agricultural use, but are also precursors to many nerve agents used in chemical warfare.

If successful, the project will see epigenomic analysis delivered in a man-portable device that requires minimal training for operation. This would enable global access to an analytical capability previously restricted to permanently-based biological sampling laboratories, often located in limited places. It would also allow real-time surveillance of emerging threats, particularly biological ones, to be performed from forensic evidence collection on the battlefield.

AMINO ACID OF THE WEEK

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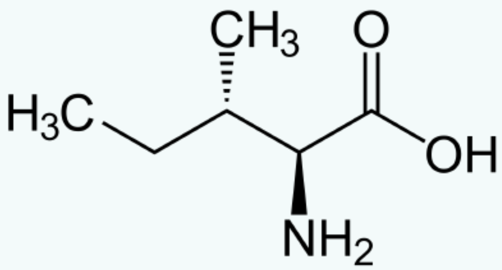
[ISOLEUCINE]

CHEMICAL STRUCTURE



ISOLEUCINE

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RNA CODONS A U H

NON-POLAR.

UNCHARGED AT PHYSIOLOGICAL pH.

BUILDING BLOCK OF PROTEINS.

DISCOVERED IN 1903 BY GERMAN CHEMIST FELIX EHRLICH. ISOLATED FROM HEMOGLOBIN PROTEIN.

FOODS RICH IN ISOLEUCINE INCLUDE EGGS, SOY PROTEIN, SEAWEED, TURKEY, CHEESE AND FISH.

ESSENTIAL; CANNOT BE SYNTHESISED BY HUMANS.

ASSOCIATED WITH INSULIN RESISTANCE: HIGHER ISOLEUCINE LEVELS OBSERVED IN DIABETICS.

GLUCOGENIC AND KETOGENIC.

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Contact us

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We also encourage anyone to share with us anything you'd like us to take a look at, be it a bioinformatics tool that you have made or find useful; or news in the bioinformatics world that you'd like to see written about in future issues.

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