Barriers and Opportunities: Science, Technology, Disarmament and Non-proliferation

2nd Annual Global Forum on Scientific Advances Important to the Biological and Toxins Weapons Convention
Palais de Nations, Geneva, Switzerland
2 December 2019

Jonathan E. Forman, Ph.D.
Science Policy Adviser and Secretary to the Scientific Advisory Board
Where Does Science Fit Into An International Disarmament and Non-Proliferation Treaty?
Where Does Science Fit Into An International Disarmament and Non-Proliferation Treaty?
The Conventions Mandate the States Parties to Discuss Science

The Conference of States Parties Shall:

“Review scientific and technological developments that could affect the operation of this Convention and, in this context, direct the Director General to establish a Scientific Advisory Board to enable him, in the performance of his functions, to render specialized advice in areas of science and technology relevant to this Convention, to the Conference, the Executive Council or States Parties.”

*CWC Article VIII, Section B, paragraph 21(h)*
The Conventions Mandate the States Parties to Discuss Science

CWC Article VIII, Article XII

Five years after the entry into force of this Convention, or earlier if it is requested by a majority of Parties to the Convention by submitting a proposal to this effect to the Depositary Governments, a conference of States Parties to the Convention shall be held at Geneva, Switzerland, to review the operation of the Convention, with a view to assuring that the purposes of the preamble and the provisions of the Convention, including the provisions concerning negotiations on chemical weapons, are being realised. Such review shall take into account any new scientific and technological developments relevant to the Convention.
How Do 193 “States Parties” Discuss Science?

Signed Without Ratification

Non-Signatory
How Do 193 “States Parties” Discuss Science?
How Do 193 “States Parties” Discuss Science?
How Do 193 “States Parties” Discuss Science?

Is it any clearer amongst the 183 States Parties to the BTWC?

Signed Without Ratification  Non-Signatory
Can the Science Connect to Policy Priorities?

- **Science**: discovery, evidence, knowledge (running experiments)

- **Policy**: values and norms (defining outcomes)
Can the Science Connect to Policy Priorities?

- **Science:** discovery, evidence, knowledge (running experiments)

- **Policy:** values and norms (defining outcomes)

Our desired outcomes: Eliminate chemical and biological weapons!
THE BOOK OF
TOTALLY
IRRESPONSIBLE
SCIENCE

FEATUREING
★ How to Grow a
Frankenstein Hand!
★ How to Turn Milk
into Stone!
★ How to Make a
Potato Gun!

PLUS
★ Cola Geysers!
★ Burning Ice!
★ DIY Blubber!
★ Homemade
Lightning!
★ And More...

64 DARING
EXPERIMENTS
The Conventions Mandate the States Parties to Discuss Science

CWC Article VIII, Section B, paragraph 21(h)

"Review scientific and technological developments that could affect the operation of this Convention and, in this context, direct the Director General to establish a Scientific Advisory Board to enable him, in the performance of his functions, to render specialized advice in areas of science and technology relevant to this Convention, to the Conference, the Executive Council or States Parties."

Where does it say “benefit” or “challenge”? Where does it say “chemistry” or “biology”? Such review shall take into account any new scientific and technological developments relevant to the Convention.
Treaty Implementation

“The Convention”

Disarmament (Destruction and Verification)

Non-proliferation (Verification)

International Cooperation

Assistance and Protection against CWs
Treaty Implementation

“The Convention”
Treaty Implementation

“The Convention”

Obligation of both CWC and BTWC

CWC Article XI
BTWC Article X

A more difficult discussion amongst CWC and BTWC communities!

CWC Article X
BTWC Article VII
Without a Sound Scientific Basis There is No Treaty Implementation!
Without a Sound Scientific Basis There is No Treaty Implementation!
What Science Should be Our Priority?
What Science Should be Our Priority?
What Science Should be Our Priority?

Transdisciplinary and More Than (Bio)Chemicals
The real cost of sequencing: scaling computation to keep pace with data generation

Paul Muir1,2, Shantao Li1, Shakoe Lou1,2, Dafeng Wang1,2, Daniel J Spakowitz1,2, Leonidas Salichos1,2, Jing Zhang1,2, George M. Weinstock1,2, Farren Isaacs1,2, Joel Rozowsky2 and Mark Gerstein1,2,

Abstract
As the cost of sequencing continues to decrease and the amount of sequence data generated grows, new paradigms for data storage and analysis are increasingly important. The relative scaling behavior of these evolving technologies will impact genomics research moving forward.

History from the 50s to next generation sequencing
In the 1950s, the contemporaneous development of biopolymer sequencing and the digital computer started a digital revolution in the biosciences. Then in the late 1970s, the advent of the personal computer (PC) and Sanger sequencing led to an appreciable amount of sequence data being generated, stored in databases, and conceptualized within a computational framework [1–4]. Communal sequence databases were developed in the 1980s [5, 6], but most investigators worked with data of a scale that allowed transfer to and processing on a local client. In the 1990s, the rise of the Internet facilitated increased data sharing, and analysis techniques began to shift to programs hosted on websites [7]. In the mid-2000s, the most recent big change occurred with the advent of cloud computing and next generation sequencing (NGS), which led to a dramatic increase in the scale of datasets (Fig 1) [8, 9]. This necessitated changes in the storage infrastructure; databases such as the European Nucleotide Archive [9] and the Sequence Read Archive (SRA) [10] were created to store and organize high-throughput sequencing data. The SRA has grown significantly since its creation in 2007, and it now contains almost four petabases (4 x 10^21 bases), approximately half of which are open access [11]. These datasets present a challenge because they are too large for the old sharing and analysis paradigms, but recent innovations in computational technologies and approaches, especially the rise of cloud computing, provide promising avenues for handling the vast amounts of sequence data being generated.

Organizing principles for biocomputing history
There are a number of key concepts to keep in mind when considering the coevolution of sequencing and computing. First is the idea that scientific research and computing have progressed through a series of discrete paradigms driven by the technology and conceptual frameworks available at the time, a notion popularized by Jim Gray from Microsoft [12]. Gray organized his views into four paradigms of scientific research. The first two paradigms are empirical observation and attempts to identify general theories. Gray’s third paradigm describes the original type of scientific computing, epitomized by large supercomputer-based calculations and modeling, for example, computing a rocket trajectory from a set of equations. This approach tends to favor differential equations and linear-algebraic types of computations.

The fourth paradigm is much more data intensive. Here the “capture, curation, and analysis” of large amounts of information fuels scientific research [12]. Researchers often try to find patterns in “big data” and a premium is placed on resource interoperability and statistical pattern finding. In order to realize fully the potential of this approach to science, significant investment must be made both in the computational infrastructure that supports data processing and sharing and in
There is always more to the Story..
Where are the Rapid Advances in Science Happening?

Scientific Publications in 2014 (from UNESCO Science Report)

Current estimate of global scientific publications is > 2.5 million papers/year
Where are the Rapid Advances in Science Happening?

Patent Application by origin 2017


Current estimate of global patent applications is > 3 million/year
Where are the Rapid Advances in Science Happening?

Patent Application by Location of (Assigned) Inventor

- Japan
- U.S.
- Germany
- Republic of Korea
- China
- Other origins

Where are the Rapid Advancements in Science Happening?

Scientific Publications in 2014 (from UNESCO Science Report)

Patent Application by origin 2017


Regulated markets and sectors – commonly operating beyond the borders of the traditional non-proliferation communities

Continuation of driving forces reported in 2016 by OECD
Commercial/Private Sector Driving Forces are Significant

**CRISPR technology: global market forecasts from 2017 to 2023**

(Source: CRISPR Technology & Market Overview: from Lab to Industry 2018 report, Yole Développement, October 2018)

\[ \text{CAGR}_{2017-2023} \approx 44\% \]
Commercial/Private Sector Driving Forces are Significant

Top 3 of the most well-funded CRISPR companies

- **Editas Medicine**
  - Total Funding: $163M
  - 2013: $43M

- **CRISPR Therapeutics**
  - Total Funding: $162M
  - 2014: $25M
  - 2015: $64M
  - 2016: $30M

- **Intellia Therapeutics**
  - Total Funding: $85M
  - 2014: $15M
  - 2015: $70M

(CAGR = compound annual growth rate)
Commercial/Private Sector Driving Forces are Significant

Top 3 of the most well-funded CRISPR companies

- **editas MEDICINE**
  - Total Funding: $163M
  - Market capacity: 29 November 2019
    - CRISPR biotech market: $1.5 Billion

- **CRISPR THERAPEUTICS**
  - Total Funding: $162M
  - Market capacity: 29 November 2019
    - CRISPR therapeutics market: $3.76 Billion

- **Intellia THERAPEUTICS**
  - Total Funding: $85M
  - Market capacity: 29 November 2019
    - CRISPR agro market: $0.83 Billion

(CAGR = compound annual growth rate)
CRISPR enters its first human clinical trials

The gene editor targets cancer, blood disorders and blindness

CUTTING ROOM Scientists will soon wield the molecular scissors CRISPR/Cas9 in the human body. Some people with a form of inherited blindness will have the gene editor injected into their eyes, where researchers hope it will snip out a mutation. Two other trials are CRISPR editing cells outside of the body to treat cancer or blood disorders.

TRAFFIC_ANALYZER/GETTY IMAGES PLUS
Commercial/Private Sector Driving Forces are Significant (CAGR = compound annual growth rate)
Technological Change is More Than (Bio)Chemistry

Most important technologies by 2022

Emerging Technologies?

Information Technologies
  Software
  Artificial Intelligence
  Big Data
  Bioengineering/Biology
  Robotics/Automation
  Additive Manufacturing

Nanotechnology
Sustainability
Medical Diagnostics/Healthcare
Cloud Computing
Renewable Energy
Bionanotechnology
Genomics/Proteomics
Embedded Processing
Space Technologies
Quantum Computing

These are technologies NOT applications!
“Important Technologies” and Chemistry

Nature 2017, 549, 445–447
DOI: 10.1038/549445a
How to explore chemical space using algorithms and automation

Piotr S. Grómski, Alon B. Henson, Jaroslaw M. Granda & Levy Cronin

Nature Reviews Chemistry 3, 119-128 (2019) | Download Citation

Abstract

Although extending the reactivity of a given class of molecules is relatively straightforward, the discovery of genuinely new reactivity and the molecules that result is a wholly more challenging problem. If new reactions can be considered unpredictable using current chemical knowledge, then we suggest that they are not merely new but also novel. Such a classification, however, requires an expert judge to have access to all current chemical knowledge or risks a lack of information being interpreted as unpredictability. Here, we describe how searching chemical space using automation and algorithms improves the probability of discovery. The former enables routine chemical tasks to be performed more quickly and consistently, while the latter uses algorithms to facilitate the searching of chemical knowledge databases. Experimental systems can also be developed to discover novel molecules, reactions and mechanisms by augmenting the intuition of the human expert. In order to find new chemical laws, we must seek to question current assumptions and biases. Accomplishing that involves using two areas of algorithmic approaches: algorithms to perform searches, and more general machine learning and statistical modelling algorithms to predict the chemistry under investigation. We propose that such a chemical intelligence approach is already being used and that, in the not-too-distant future, the automated chemical reactor systems controlled by these algorithms and monitored by a sensor array will be capable of navigating and searching chemical space more quickly, efficiently and, importantly, without bias. This approach promises to yield not only new molecules but also unpredictable and thus novel reactivity.
How Does Science and Technology Fit Into All of This?

“Important Technologies” and Chemistry

How to explore chemical space using algorithms and automation

Although extending the reactivity of a given chemical system is relatively straightforward, the discovery of new molecules is hard due to the vastness of chemical space. The molecules that result is a whole are not only unpredictable but also unknown, and their reactions can be considered unexplored territory. If all the knowledge, then we suggest that such discovery is novel. Such a classification, however, is not a guarantee that access to all current chemical knowledge is being interpreted as unpredictable chemical space. The probability of discovery. The former can be performed more quickly and conveniently than the latter using algorithms to facilitate the search.

Experimental systems can also be used to explore chemical space, molecules, reactions, and mechanisms that are not visible to the human expert. In order to find the real chemical system, we have to question current assumptions and not just use two areas of algorithmic approach: high throughput searches, and more general machine learning algorithms to predict the chemistry. The question is whether such a chemical intelligence is here, or will we be able to build that, in the not-too-distant future, all the chemical systems controlled by these algorithms in the array will be capable of navigating chemical space quickly, efficiently and, importantly, non-repetitively. This promises to yield not only new molecules but also unpredictable and thus novel reactivity.

Chem 5, 2019, 1–14
DOI: 10.1016/j.jchempr.2018.12.004
How Does Science and Technology Fit Into All of This?

Nature 2017, 549, 445–447
DOI: 10.1038/549445a

Important Technologies” and Chemistry

Chem 5, 2019, 1–14
DOI: 10.1016/j.chempr.2018.12.004

Faster and more efficient way to medical countermeasures?
Central Nervous System (CNS)-Acting Chemicals

Dexmedetomidine
Mechanism of action:
- Sympathetic chain blockade
- Partial agonist at 
  
  
- Inhibits calcium ion influx
- Reduces PNAP

Clonidine
Mechanism of action:
- Reduces release of noradrenaline at both central and peripheral sympathetic nerve terminals
- Reduces release of noradrenaline at both central and peripheral sympathetic nerve terminals
- Inhibits calcium ion influx
- Reduces PNAP

Fentanyl
- Fentanyl and its analogues are mu-receptors that require association for opioideffect.
- Route of entry for fentanyl includes the oral cavity, subcutaneous tissue, and bone.
- Fentanyl and its analogues are mu-receptors that require association for opioideffect.
- Route of entry for fentanyl includes the oral cavity, subcutaneous tissue, and bone.

Inhaled anaesthetic examples
Mechanism of action:
- Inhibits pre-synaptic GABA release
- Increases intracellular chloride, producing a paralyzing effect on the motor axon
- Inhibits pre-synaptic GABA release
- Increases intracellular chloride, producing a paralyzing effect on the motor axon

BZ (3-quinuclidinyl benzilate)
Properties:
- Causes convulsions and seizures in animal tests.
- Causes convulsions and seizures in animal tests.

Safetynet of BZ
- The safety net prevents accidental exposure to BZ.
- The safety net prevents accidental exposure to BZ.

Dose in [mg/ml/m2]
Mechanism of action:
- Acts as an agonist at the benzodiazepine receptor.
- Acts as an agonist at the benzodiazepine receptor.

Toxicity
- Effects:
  - Loss of consciousness
  - Amnesia
  - Reappearance after 20 minutes
  - Reappearance after 20 minutes
  - Loss of consciousness
  - Amnesia

Antidote: Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
- Naloxone hydrochloride
## READY TO BE DEPLOYED NOW

<table>
<thead>
<tr>
<th>Virtual assistants (natural language based)</th>
<th>Datascience-based maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI-based pricing engines</td>
<td>Blockchain-based supply chain track &amp; trace</td>
</tr>
<tr>
<td>AI-based next best actions in marketing</td>
<td>Virtual assistant-based internal administration</td>
</tr>
<tr>
<td>AI-based augmentation of control room operators</td>
<td>Robotic process automation in administration</td>
</tr>
<tr>
<td>AI-based experiment prediction &amp; evaluation</td>
<td>...and so much more...</td>
</tr>
</tbody>
</table>
New ways to approach problem solving and change organizational cultures!
POWERING ON-DEMAND DISCOVERY BIOLOGY

ACCELERATING DRUG DISCOVERY AND SYNTHETIC BIOLOGY RESEARCH

The Transcriptic Common Lab Environment (TCLE) coordinates scientific processes, instruments, and robotics to create a programmatically addressable lab environment that enables unparalleled scale, efficiency, and accuracy for the discovery process.

https://www.transcriptic.com/

“A Cloud Laboratory Research Service”
With a “physical” location and real equipment and people to maintain it!
Does it Look Like a Contract Research Organization?

This is not a new thing! Perhaps the answers to concerns about this are found in existing business models of CRO’s?
Policy, Regulation and/or Oversight for Science?
International Obligations and Member State Compliance

- **Treaty** = Agreement between states
- **National Compliance** = laws and regulations
  - States Parties must establish a “National Authority”
  - National legislation
  - Criminal laws, trade monitoring, reporting and enforcement
International Obligations and Member State Compliance

- Treaty = Agreement between states
We Cannot Afford to Fear Science!
All of this Advanced Science and...

- Chemical weapons being used
All of this Advanced Science and...

- Chemical weapons being used
All of this Advanced Science and...

- Chemical weapons being used
- Biological weapons being used?
All of this Advanced Science and...

- Chemical weapons being used
- Biological weapons being used?
All of this Advanced Science and...

- Chemical weapons being used
- Biological weapons being used?
All of this Advanced Science and...

- Chemical weapons being used
- Biological weapons being used?
Reproducibility and Replicability in Science
Chemical weapons being used

Biological weapons being used?

All of this Advanced Science and…

MIT News
ON CAMPUS AND AROUND THE WORLD

A new technique developed at MIT can edit DNA in precise locations.
Graphic: Christine Daniloff/Mit

Editing the genome with high precision
New method allows scientists to insert multiple genes in specific locations, delete defective genes.

Anne Trafton, MIT News Office
January 3, 2013
A New Gene Editing Tool Could Make CRISPR More Precise

Prime editing offers a new way to make changes to DNA while avoiding some of the drawbacks and clunkiness of traditional CRISPR.

Unlike classic CRISPR-based editing, which fully cleaves DNA in two, prime editing starts with a cut to only one strand of the double helix. (Perception7 / iStock)

By Lila Thulin
SMITHSONIAN.COM
OCTOBER 21, 2019
Uncertainty...

What are the capabilities (independent of technology) we need?

What Scenarios Do We Need to be Prepared for?
Once you answer these questions, you can talk about science and technology...

Focus on needs and capability requirements...

What technologies vs. old technology?

New technology? What works reliably?

What do we need?

What scenarios do we need to be prepared for?
Recognize when something is “not right”

Further investigate as needed
“The signs are that the bombs were made with the windows open but the net curtains taped to the walls to avoid being seen. The fumes had killed off the tops of plants just outside the windows”
- Report of the Official Account of the Bombings in London on 7th July 2005
There is no shortage of data being collected with possible application to recognizing the “unusual”
Timeline of wearables: a little bit of history

(Source: Medical Wearables: Market and Technology Trends 2019 report, Yole Développement, March 2019)

1788
Thomas Jefferson introduced the first pedometer to the US

1938
Aurex Corp developed the 1st wearable hearing aid

2000
Fitness tracking

2009
Activity trackers, wireless enables wearable technology

2012
Proteus Digital Health developed an ingestible sensor approved by the FDA in 2012 to improve patients habits

2019
Apple launched the first approved ECG integrated in smartwatch

Next step: Medical devices more conformable

Single function
Thomish Meter

Multi-function
Hearing aid

Medical-functions
Appel’s ECG

Ingestible sensors and wearables devices
Philips lifeline

Consumer fitness and sport products enter the market starting with Bluetooth headset

Yole Développement is part of Yole Group of Companies

New technology gives early warning of exposure to disease-causing pathogens

The enabling algorithm uses non-invasive physiological data to predict the probability of viral or bacterial exposures.
Medical wearables and sensors: 2018 – 2024 market forecast (in B$)

(Source: Medical Wearables: Market and Technology Trends 2019 report, Yole Développement, March 2019)

Medical wearables:
CAGR$_{2018-2024}$ : 31%

Sensors:
CAGR$_{2018-2024}$ : 21.6%

Medical wearables segments:
- Veterinary
- Maternal & neonatal care
- Medical prevention
- Rehabilitation systems & therapeutics
- Metabolic & cardiovascular monitoring
- Respiratory & movement disorder
- Glucose monitoring & drug delivery
- Sensors for wearables

Yole Développement is part of Yole Group of Companies
Digitization transforms the Chemical Industry rapidly across its entire horizontal value chain.

- **Big-data/advanced analytics in OpEx/CapEx:** Big data-driven raw material analytics to optimize feedback loops.
- **End to end supply chain integration:** Production data sharing with suppliers/realt-time supply tracking.
- **Process automation:** Sensor-based production control and real-time optimization of YETI®.
- **Integrated lean system:** IT-based integrated lean system to drive manufacturing excellence.
- **Engineering/R&D 4.0:** Machine-learning-driven design and formulation improvements.
- **New roads to market:** Using online/marketplace sales channels.
- **Digitization of customer experience:** Customer self-service platform.

**Digital procurement tools:** Digital tools enabling more efficient procurement processes.

**Predictive maintenance:** Advanced analytics-based predictive and risk-based maintenance.

**Digital manufacturing:** Production automation by application of autonomous logistics, drone inspections.

**Risk management:** Advanced analytics-based risk management/cyber security.

**G&A 4.0:** Back office automation, e.g., no-touch orders.

**Commercial engines:** Use advanced analytics for lead generation, etc.

**PLUS:** new, radically different business models.
A Practical View of Science and Technology is Needed
A Practical View of Science and Technology is Needed
A Practical View of Science and Technology is Needed
<table>
<thead>
<tr>
<th>Country</th>
<th>Member of</th>
<th>Date of Deposit</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH</td>
<td>Switzerland</td>
<td>10/03/1995</td>
</tr>
</tbody>
</table>

**Legend**

- Western Europe and Other States (WEOG)
- Eastern Europe
- Africa
- Latin America and the Caribbean (GRULAC)
- Asia

**Order of Entry into Force**


**Country Symbol**

- **H** for Hydrogen
Scientific and Technological Change

- Uncertainty is the challenge!
- Technological change is inevitable
- *Disarmament non-proliferation cannot afford scientific illiteracy*
- We Need Innovative ideas, approaches and policies

OPCW
OPCW

Organisation for the Prohibition of Chemical Weapons
Organisation pour l'Interdiction des Armes Chimiques
Организация по запрещению химического оружия
Organización para la Prohibición de las Armas Químicas