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Spiez CONVERGENCE 2018

S&T @ crossroad of chemistry and biology

RC-4, Science for Diplomats, 23 Nov. 2018

Stefan Mogl, Beat Schmidt Spiez Laboratory





Spiez CONVERGENCE workshop series 2014 / 2016 / 2018



- Explore S&T challenges to CWC and BWC
- 3rd Review of S&T at intersection of biology and chemistry
- Participants from academia, industry, arms control

https://www.labor-spiez.ch/pdf/de/rue/Spiez_Convergence_2014_web.pdf

https://www.labor-spiez.ch/pdf/en/Report_on_the_second_workshop-5-9_September_2016.pdf

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Subjects Reviewed 2018

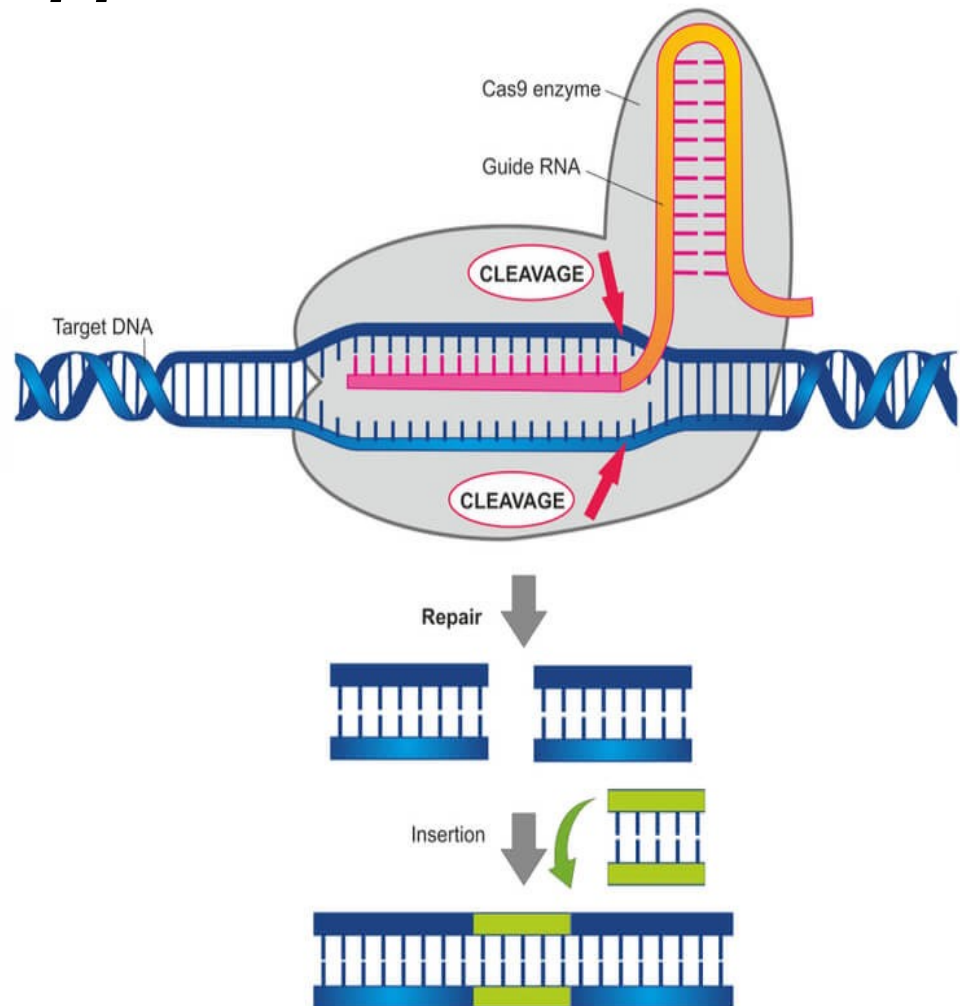
- CRISPR Genome editing
- Synthetic Biology
- Synthetic and Analytical Chemistry
- Material Sciences including Nanotechnology
- Additive Manufacturing
- Bioinformatics, Omics, and Big Data
- Policy discussion

Revisiting subjects:

- Deeper understanding of maturity
- Shows speed of progress
- Relevance
- Allows better predictions

CRISPR Genome editing: *Trends and industrial applications*

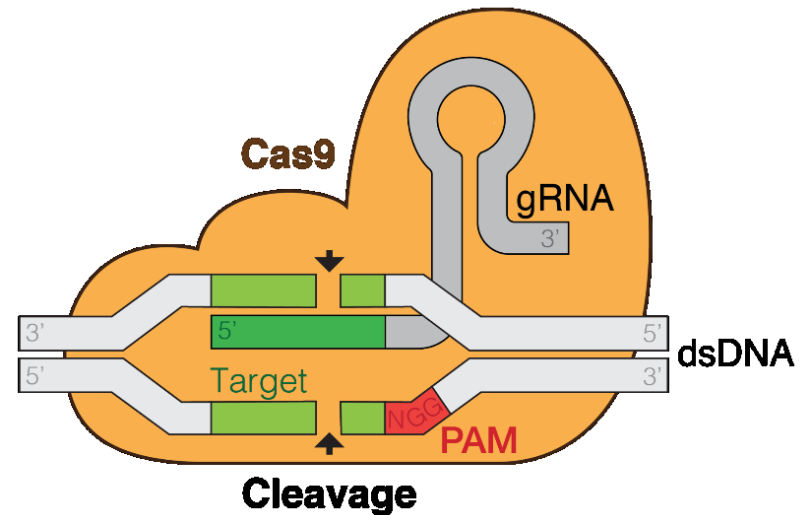
- Makes genome editing:
 - Easier
 - Faster
 - More accessible
- Target any gene
- With biocatalysts cause variety of desired modifications
- Practical applications:
 - Reversal of antibiotic resistance in bacteria
 - Development of diagnostic techniques





CRISPR Genome editing: *Trends and industrial applications*

- Many applications still at proof-of-concept stage
- Practical challenges before clinical application of CRISPR based therapeutics:
 - Delivery and off-target effects
 - Ethical issues regarding gene editing in the germ line

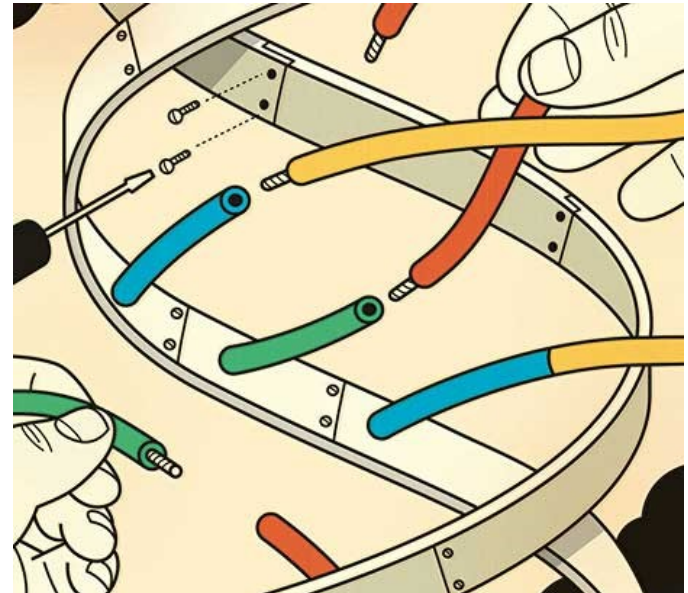




Synthetic Biology:

Trends and industrial applications

- Industry manufactures complex biomolecules using synthetic biology
- *In vitro* designs provide access to oligosaccharides, proteins, assays
- Moving to *in vivo* systems requires change from engineering design to evolution





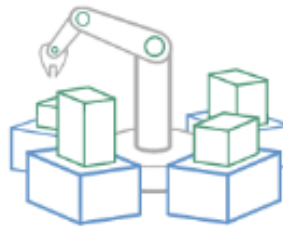
Synthetic Biology:

Trends and industrial applications

- Analysis of pathogen specific resistance processes by targeted mutagenesis
- Practical application: diagnostic tests for antibiotic resistance in bacteria
- Limitations remain to engineer biological system
- Tacit knowledge still important



1 DESIGN



2 CONDUCT



3 EXPLORE



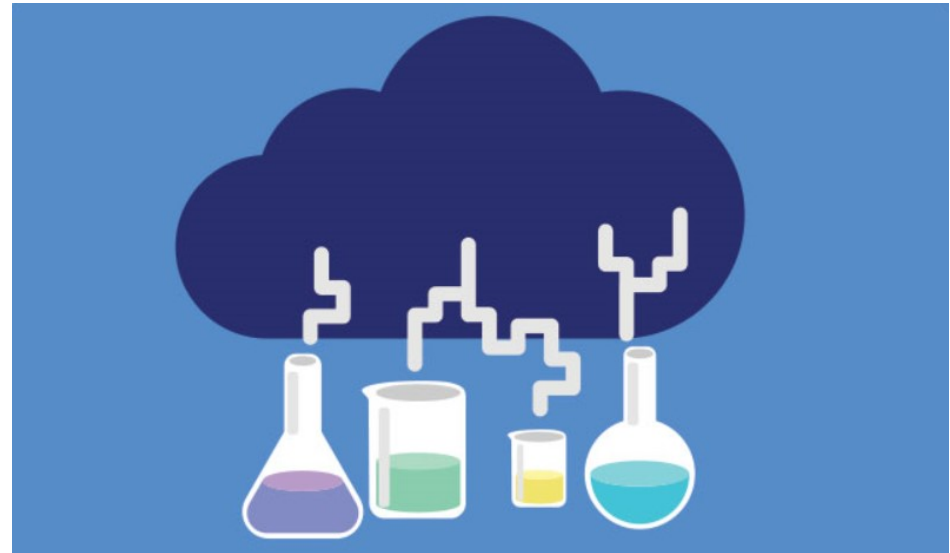
4 ANALYZE



Synthetic Biology:

Trends and industrial applications

- Cloud laboratories increase speed of synthesis
- Provide reproducible environment, standardised protocols
- Security:
 - Utilisation for malevolent purposes ?
 - Target for remote attacks ?





Synthetic and Analytical Chemistry: *Integrated continuous processing*

- Distinct advantages over batch production in chemical manufacturing
- Widely applied but not for production of pharmaceuticals
- Many advantages for pharmaceutical manufacturing
- For bio-processes, working with living organisms poses challenges



Synthetic and Analytical Chemistry: ***Integrated continuous processing***

- Supervisory Control And Data Acquisition (SCADA) systems need adaptation for bio-process monitoring and control
- Process optimization is specific for a particular production process
 - Each target molecule requires a dedicated process
- Development of continuous bio-manufacturing processes for a range of pharmaceutical products
 - Target specificity is serious obstacle



Synthetic and Analytical Chemistry:

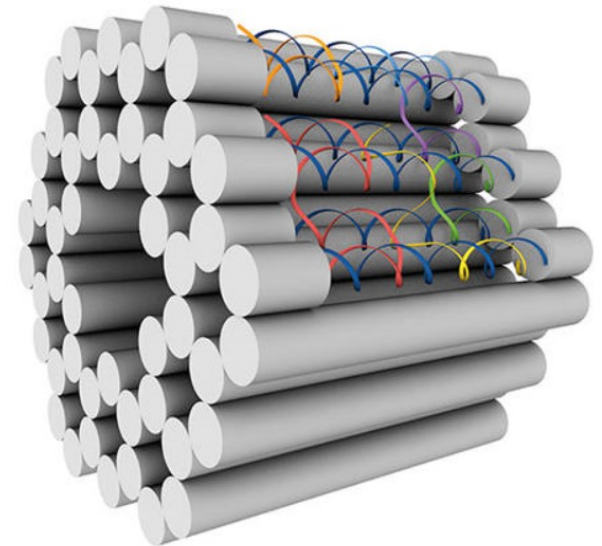
Integrated continuous processing

- Radial synthesizer as solution:
 - Automated, remotely controlled, modular assembly system
 - Manufactures several small molecules
 - Using same hardware
 - Suitable for multistep syntheses
- Centralisation of chemical synthesis:
 - Operated anywhere
 - Shift in the way chemistry is performed
 - Experiments outsourced to remote automated systems



Material Sciences: *Nanotechnology*

- DNA Origami:
 - Experiments with DNA objects as cancer therapeutics
 - Form rigid DNA structures
 - For targeted drug delivery
- Stability *in vivo* remains problematic
- Practical applications need manufacturing costs to be reduced





Material Sciences:

Nanotechnology for drug delivery

- "Functional Food":
 - Nanostructure formation by self-organization through biological systems in the body
 - Food inspired nanostructures as carrier for drugs
- Nanocarriers:
 - To improve the efficacy of drugs
 - Design stimuli responsive delivery systems

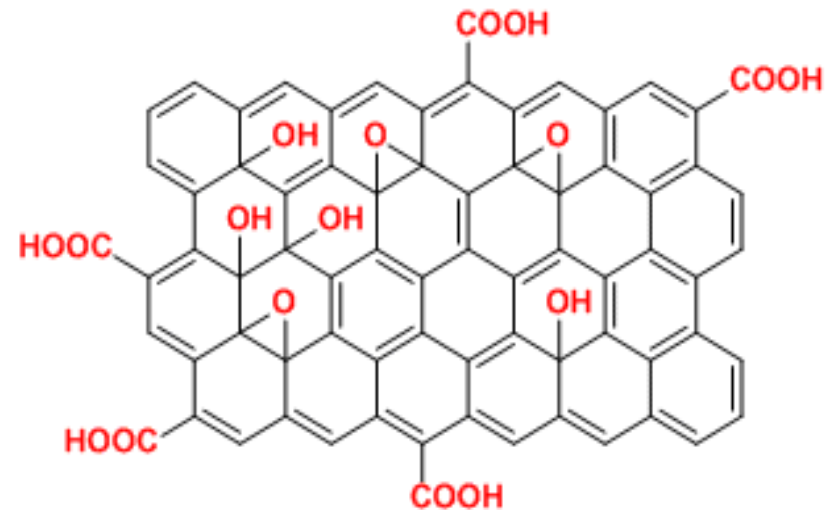




Material Sciences:

Nanotechnology for drug delivery

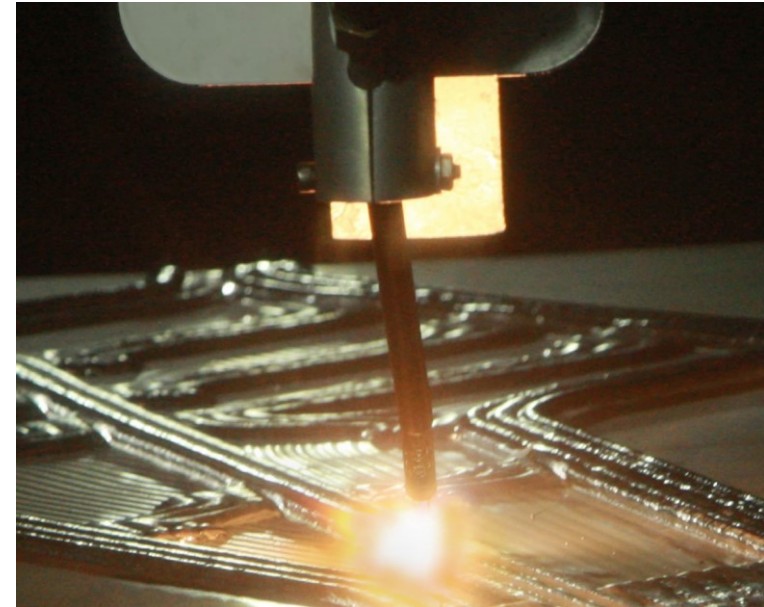
- A wide range of treatments use graphene oxides (GO)
- Two-dimensional nano-scale carbon structures
- Easy to functionalise as drug loading structure
- CBW context:
 - Nanoparticles used as aerosols and inhaled
 - Uptake through Blood Brain Barrier
 - Suitable for targeted delivery of toxins





Additive Manufacturing (AM)

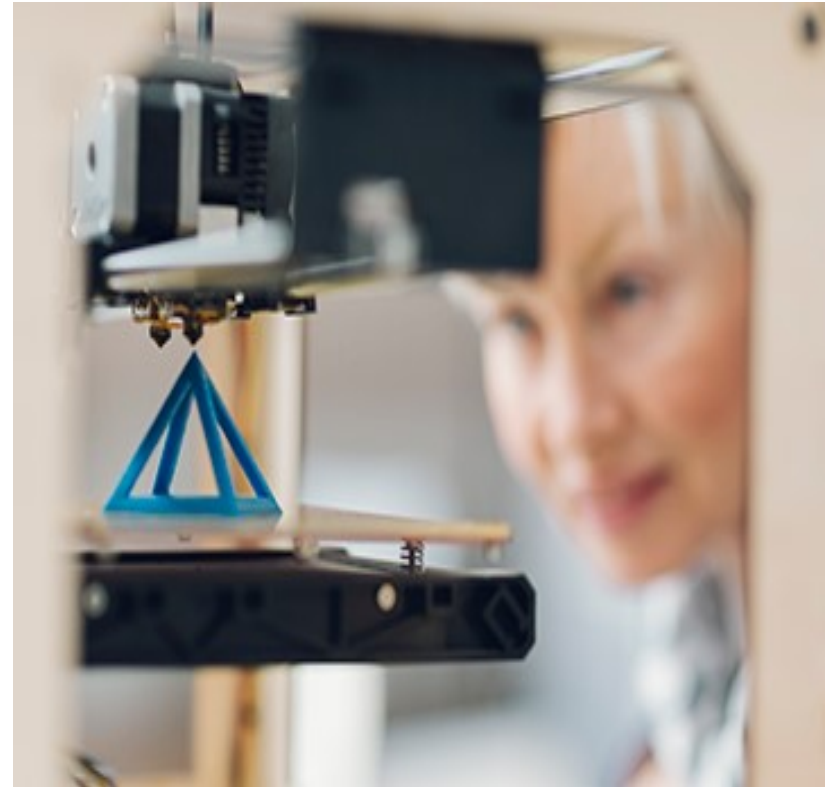
- AM industry grows rapidly
 - End user controls product design
- Different processes with range of materials available
- Faster manufacturing but cannot compete with sheet metal fabrication
- Complex parts to high performance standards remains a challenge





Additive Manufacturing (AM)

- Of interest for CBW arms control are 3D objects that withstand:
 - High temperature
 - Pressure steam sterilization
 - Highly corrosive chemicals
- Today: only industrial AM systems able to produce such high-quality parts





Additive Manufacturing (AM)

- Industrial AM systems require:
 - Professional know-how
 - Technical competence
- Unlikely, 3D printers capable of manufacturing corrosion resistant parts would be available to individuals or consumers soon
- Next 5 years:
 - List of printable materials will grow
 - AM adopted across multiple industries
 - Regulatory standards will have to be developed

Bioinformatics, 'Omics', Big Data: *Next Generation Sequencing*

- Advances driven by next-generation sequencing (NGS) techniques
 - NGS relies on DNA and RNA as information carriers
 - DNA and RNA can easily be written and read
- Performance today:
 - Parallel read operations of 10 billion molecules in single experiment
 - Precision increased to single molecule manipulations





Bioinformatics, 'Omics', Big Data: *Data Protection*

- Genomes carry information about individual:
 - Data could be used to link individual to genetic characteristics
 - Compromise privacy rights
 - Multiomics projects challenge the protection of patient-specific data
- For Data Mining: Privacy-preserving technologies need improvement





Bio informatics, Omics and Big Data

Artificial Intelligence (AI)

- AI offers way to make sense of vast amounts of data:
 - Machine Learning (ML) progressed to improve predictions with neural network architectures
 - Requires access to Big Data and high computational power
- Expl. of predictive power:
 - Reaction performances for organic syntheses
 - Builds models from simple representations of chemical and biological entities
 - Suggest structures with improved properties
 - Expands number of synthesizable materials
- Reliable safeguards need to be found and implemented



Policy discussion

Impact of S&T Advances on Treaties

- Since 2014 focus of discussions shifted:
 - From materials and equipment
 - To information, automation and remote manufacturing
- New opportunities for oversight compliance monitoring and verification





Policy discussion

Impact of S&T Advances on Treaties

- Additive manufacturing:
 - Production is moving closer to the point of use
- Bio-manufacturing of pharmaceuticals:
 - Radial synthesisers centralise chemical synthesis
- Synthetic Biology:
 - Cloud laboratories centralise lab work, separate scientist from lab experiment
- Consequences:
 - Role of end-users or actors in process is changing
 - Access to data and intangibles transfers become more relevant (regulation, control)



Policy discussion:

How would changes affect potential CBW programmes ?

- Novel CBW production facilities compared to past state programs:
 - Smaller footprint
 - Different technological features
- Non-state actors:
 - Attempts to remain opportunistic
 - Constraints: materials, equipment, agent dissemination, costs
 - Tacit knowledge
- State actor:
 - How to fit new materials and methods into contemporary CBW programme ?
 - CBW as WMD vs. sabotage, assassinations
- Are Implementation systems still effective in this changing environment ?



Policy discussion

Impact of S&T Advances on Treaties

- Multi-stakeholder approaches
 - Academia, Industry, National Authority
 - Develop Partnership and Gov. Systems
- Evaluations may have a short and longer-term perspective:
 - 3D printers could require swift response to manage risks
 - Cloud services in chemical and biological manufacturing may affect implementation over time
- Spiez CONVERGENCE wants to support assessment of S&T advances by stakeholder communities of CWC and BWC