Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Federal Office for Civil Protection FOCP
SPIEZ LABORATORY

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

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

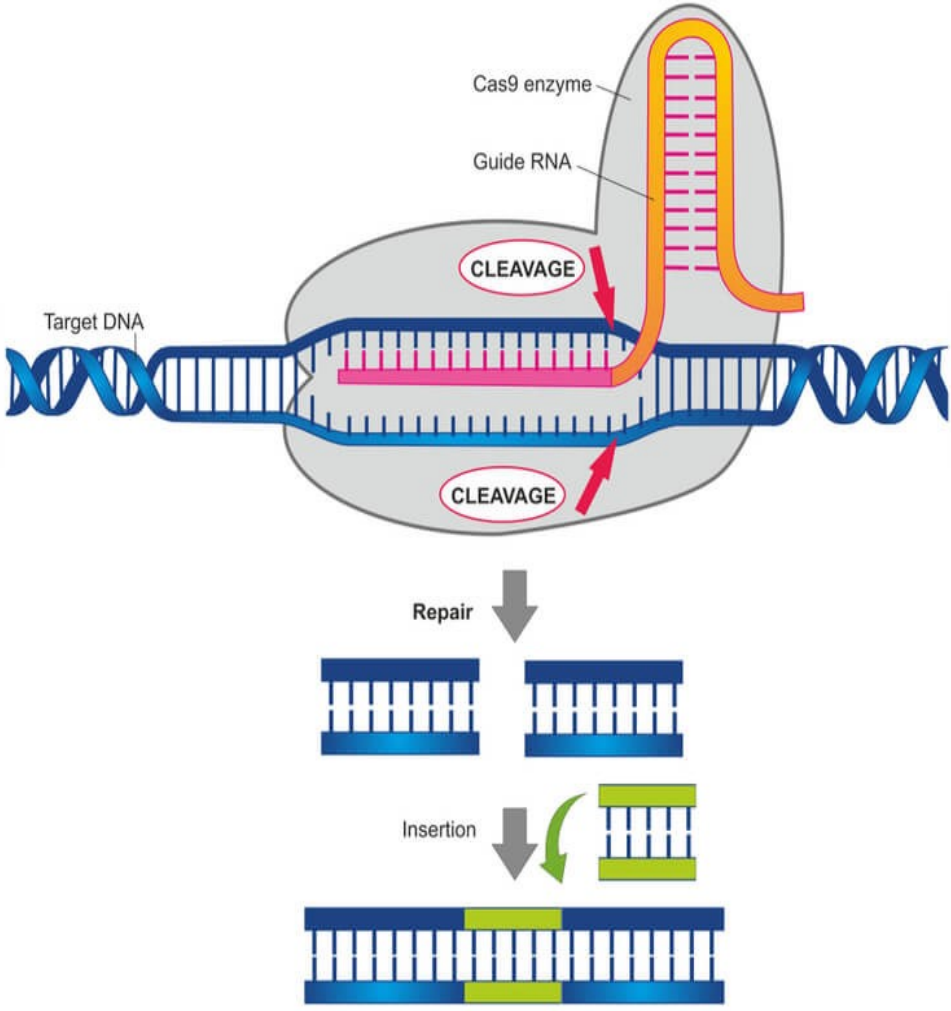


Image: https://labiotech.eu

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

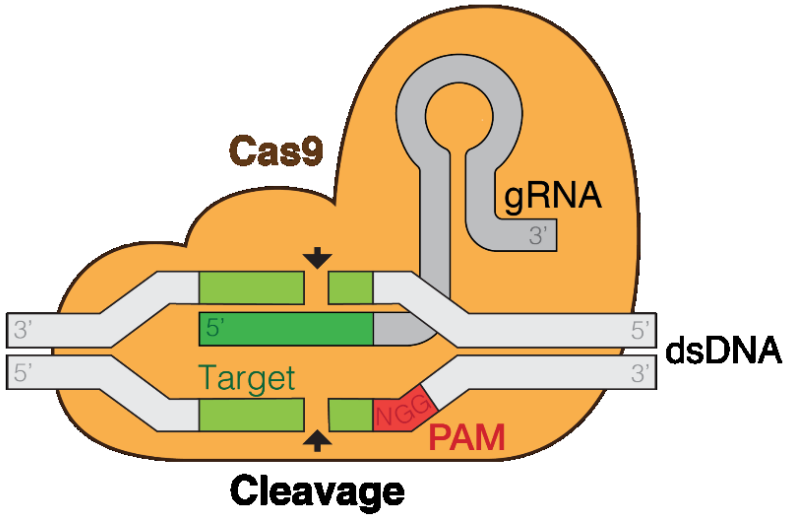
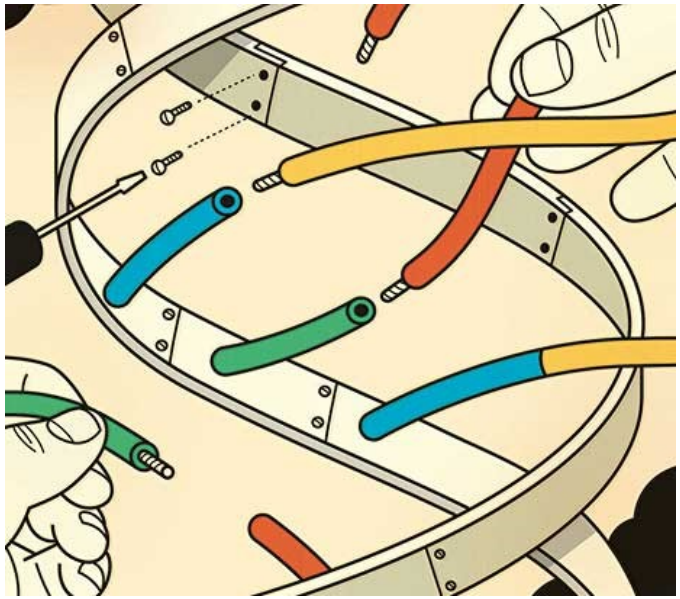


Image: http://thepigeonpress.org/

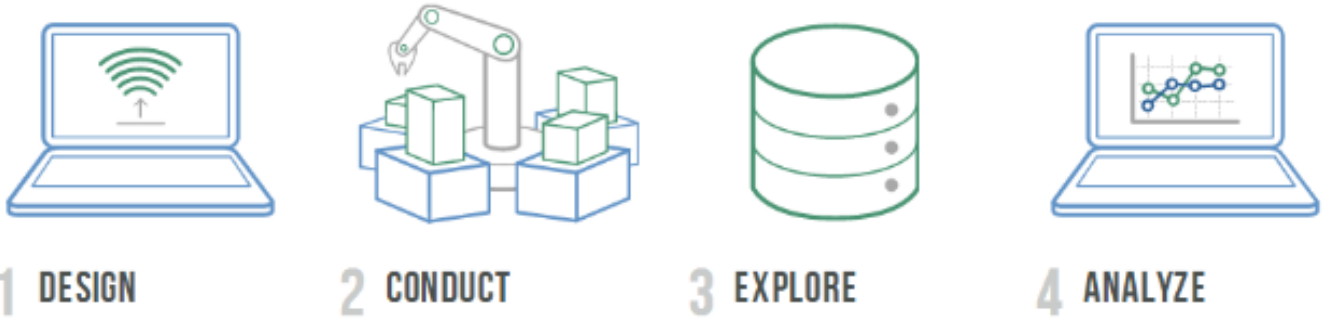
Synthetic Biology:
Trends and industrial applications

- 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



Source: www.emeraldcloudlab.com

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 ?

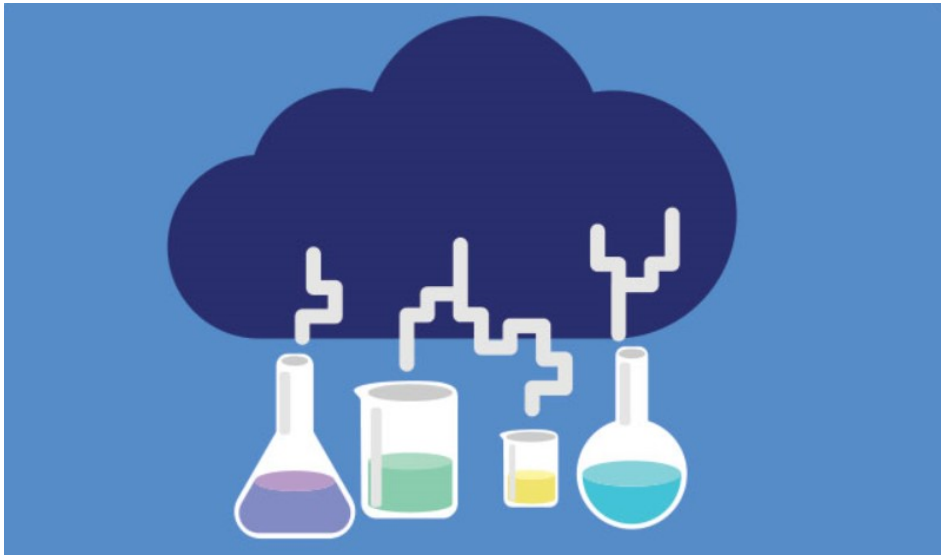


Image: https://www.the-scientist.com/bio-business/bringing-the-internet-of-things-into-the-lab

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

image: https://www.ypsofacto.com/

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

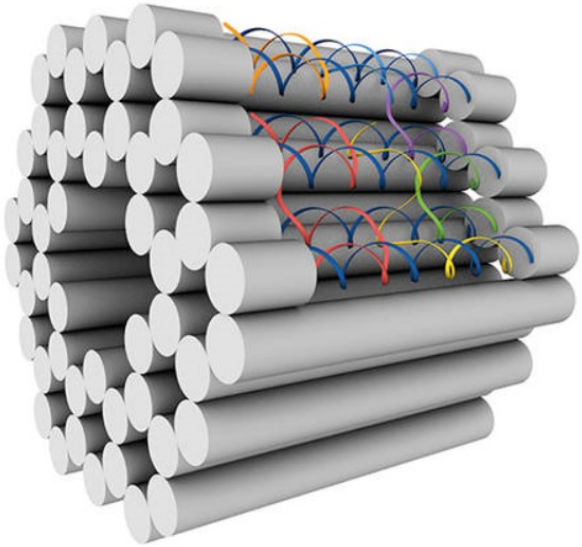


Image: https://www.tum.de/die-tum/aktuelles/pressemitteilungen/detail/article/34360/

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

Source image: https://www.asianscientist.com/

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

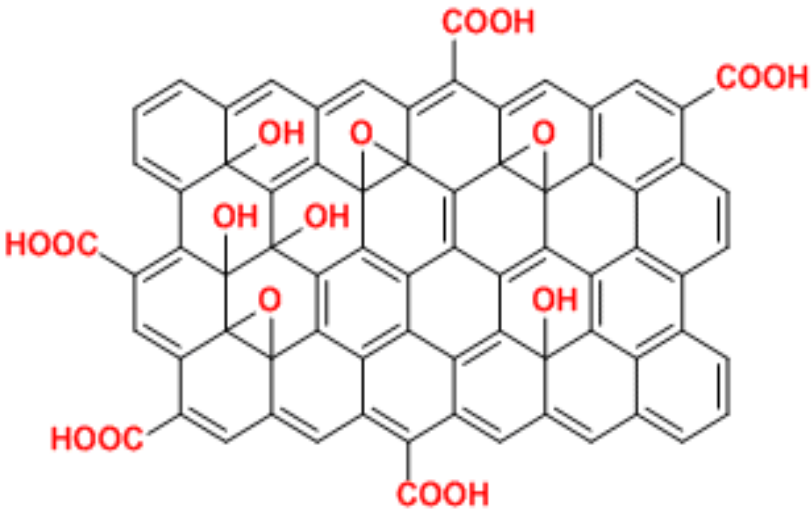


Image: https://www.tcichemicals.com/

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

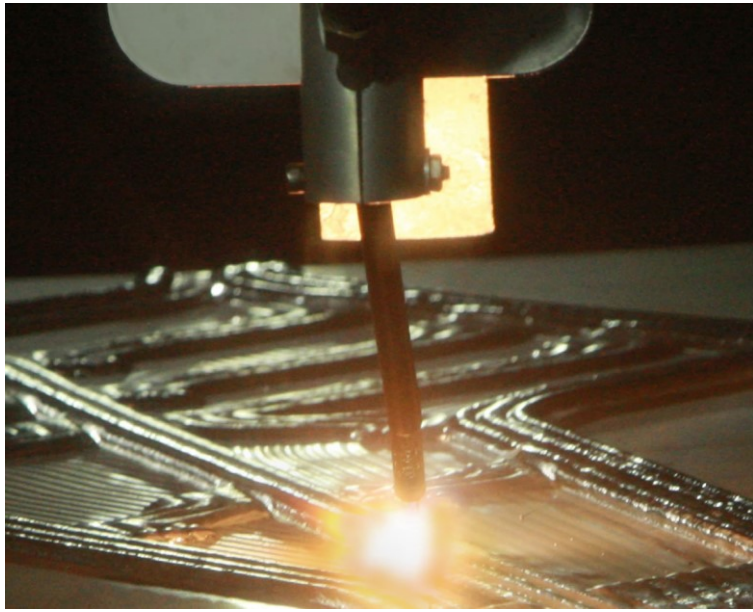


Image: www.additivemanufacturing.com

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

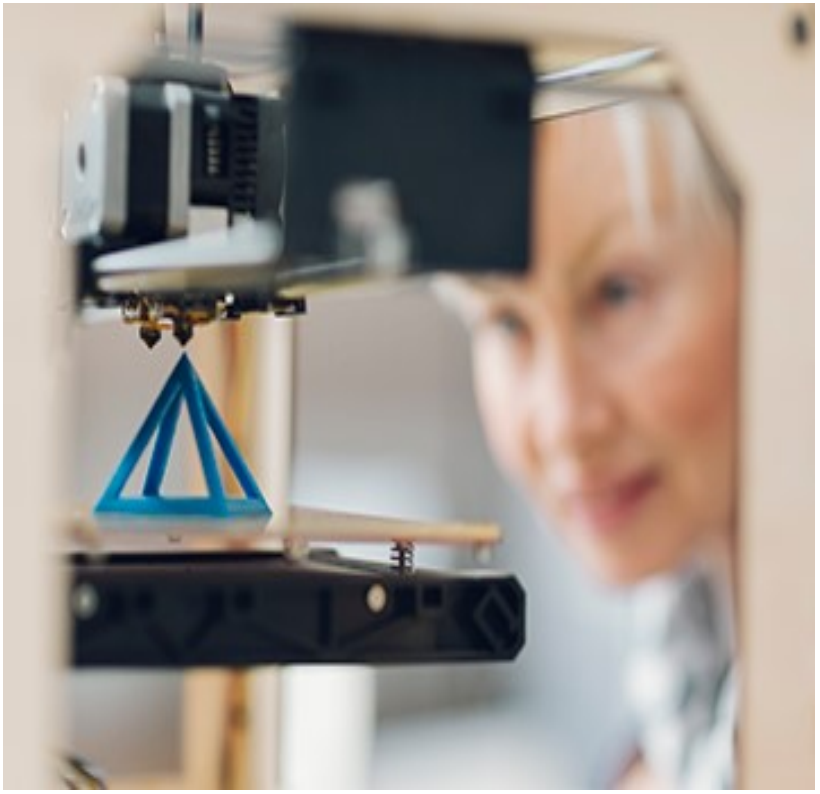


Image: https://www.dsm.com

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

Image: https://www.illumina.com

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

Image: https://www.forbes.com//

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

Image: http://rogerpielkejr.blogspot.com

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