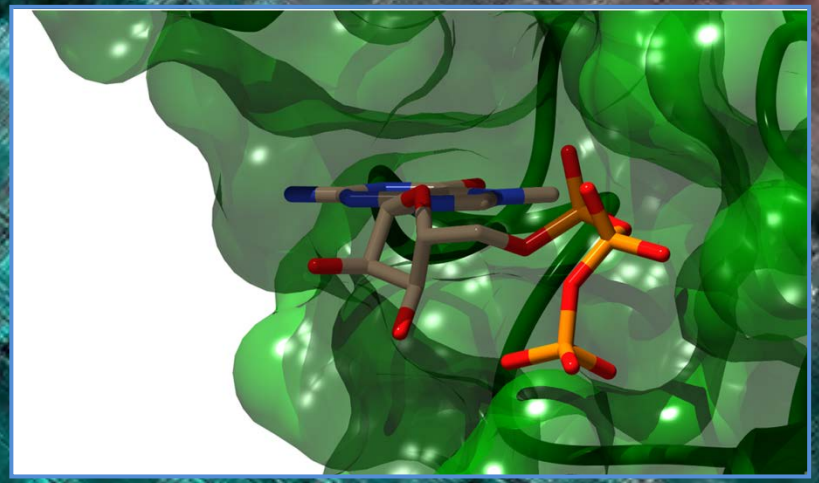
Synthetic life - beyond biology and chemistry

Marcin Ziemniak

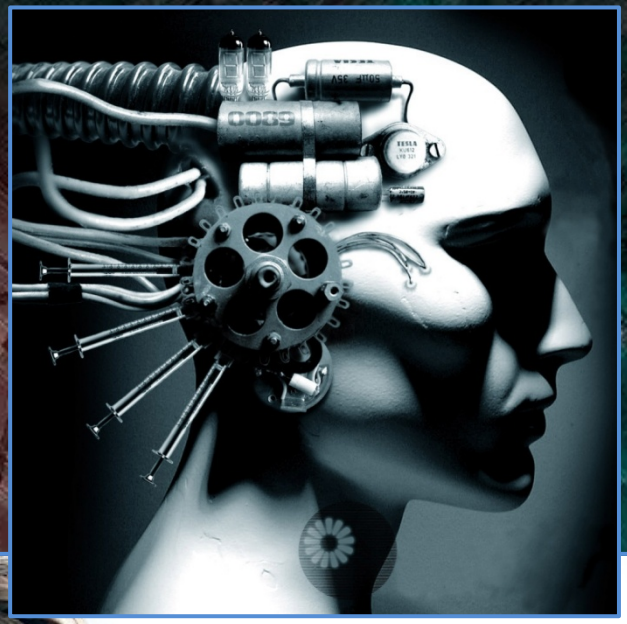
Division of Biophysics

UW

Sources of inspiration

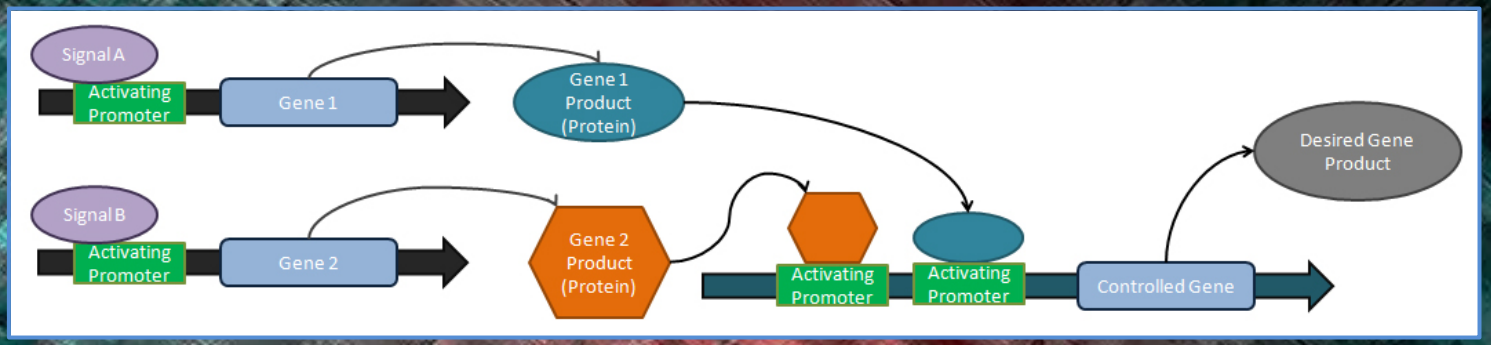


This will not be about:

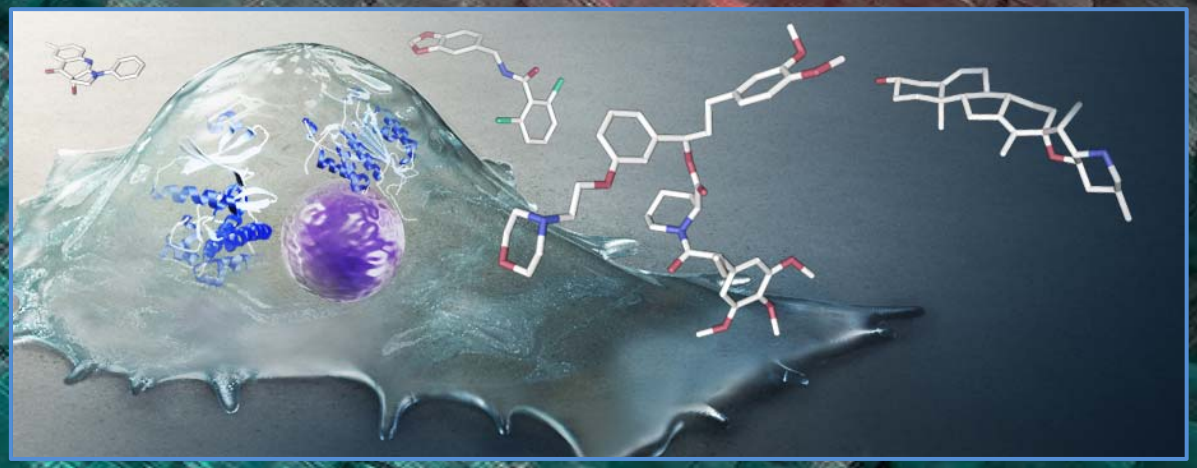


Topics

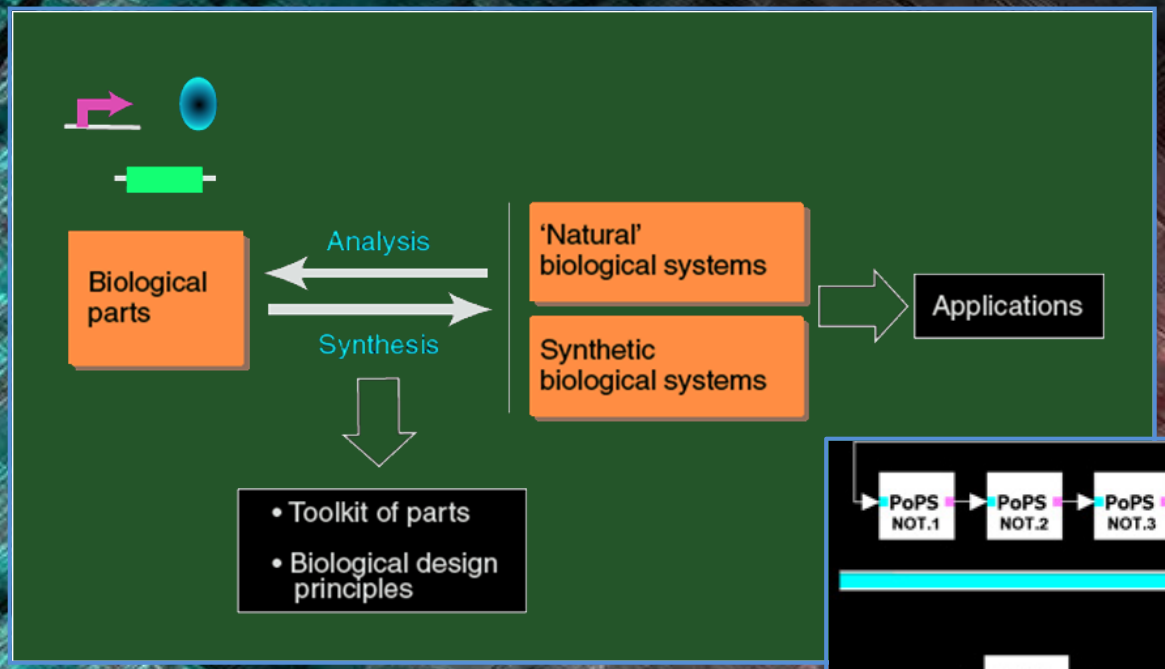
- Synthetic biology

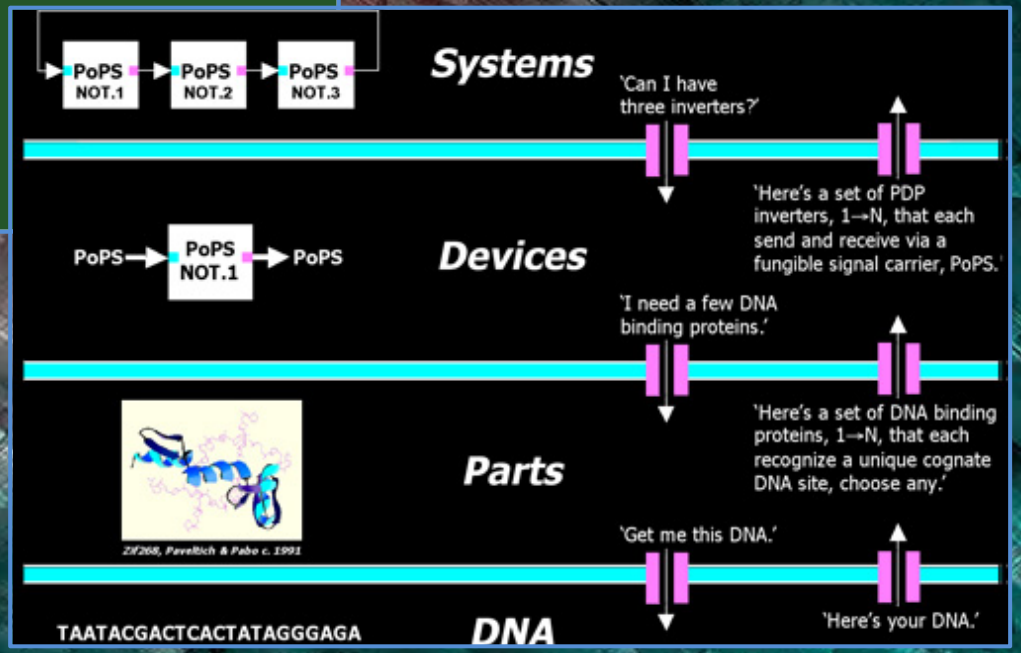


- Chemical biology (especially bioorthogonal chemistry)



Synthetic biology

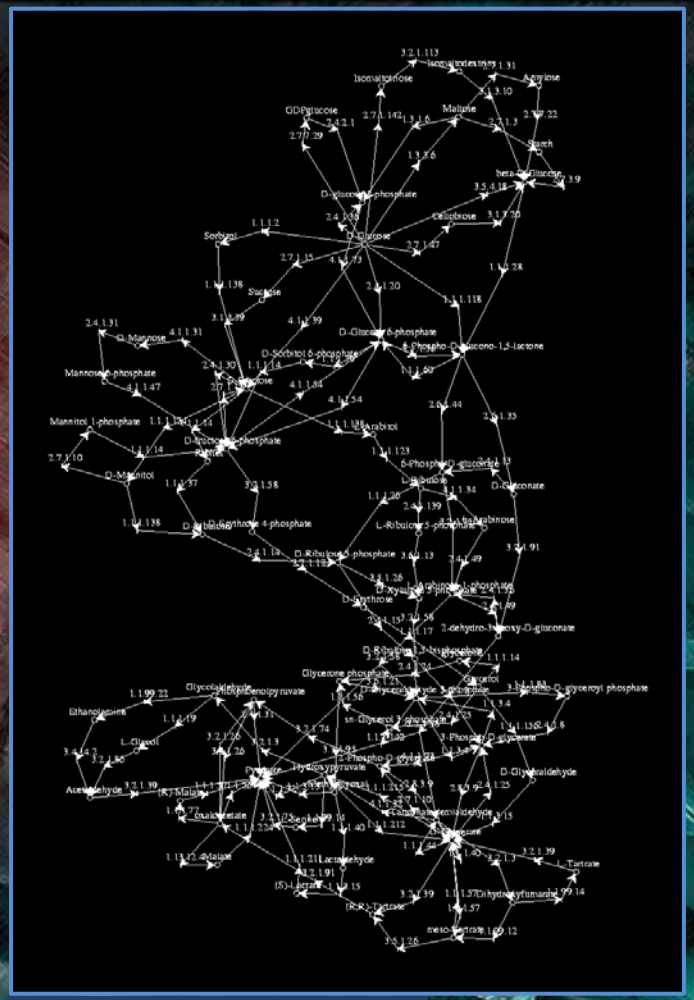




Genetic circuit – what is it?

- Biological circuit ≡ „biological pathway”
  - metabolic pathways
  - intermolecular interactions
  - gene regulation networks
  - signal transduction
  - biological neuron networks
- Nowadays some of these pathways are considered to be similar to electronic circuits and some biologists try to use them engineer a biological „devices”

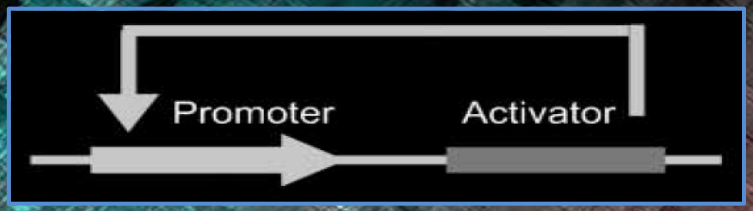
Nice dream



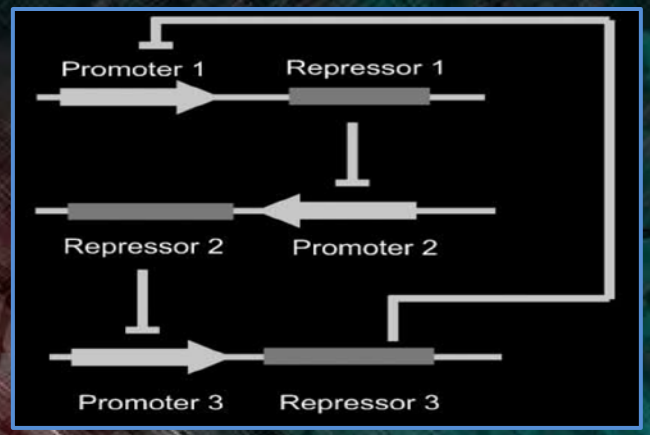
Cruel reality

Some building blocks

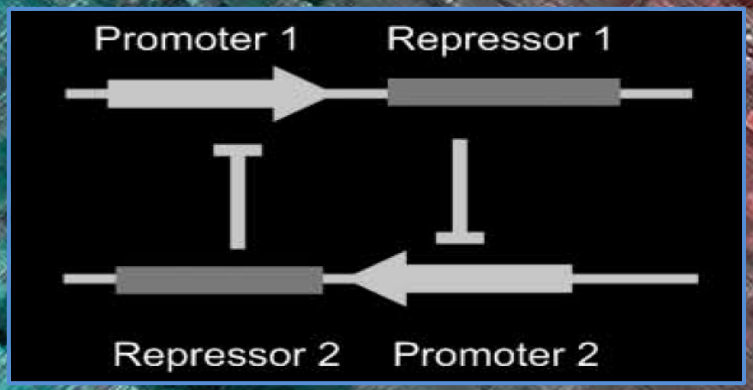
Mol. BioSyst., 2007, 3, 835–840



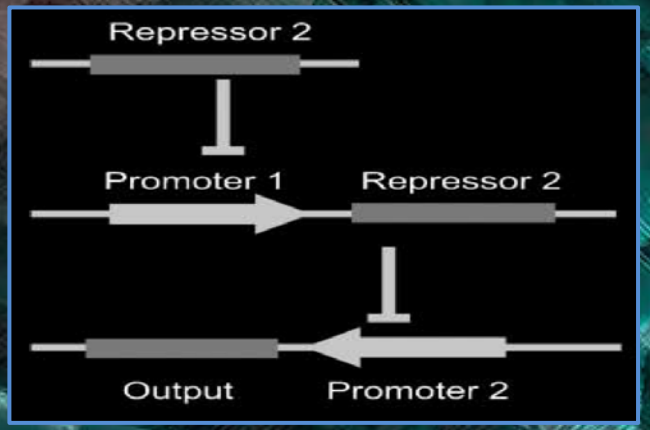
Positive force-feedback



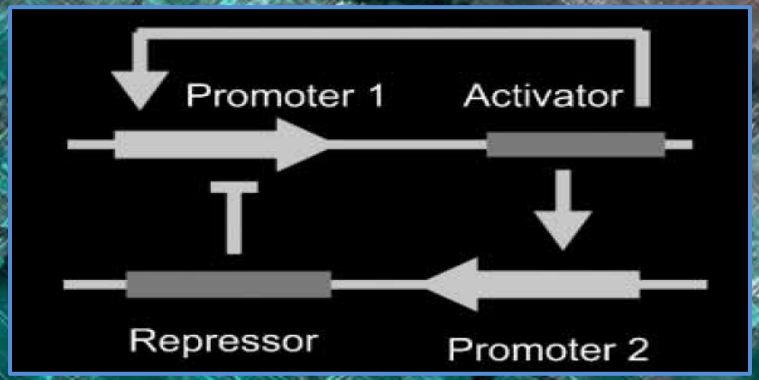
Repressilator



Genetic switch



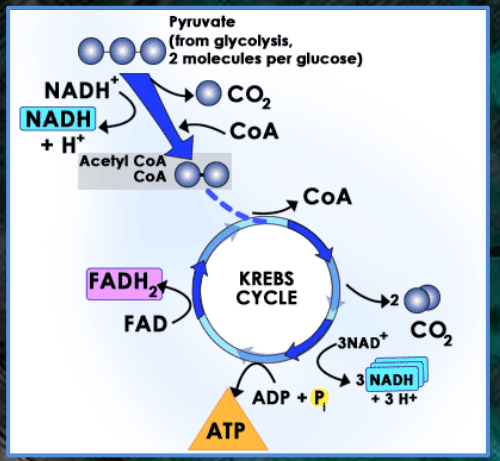
Inventer



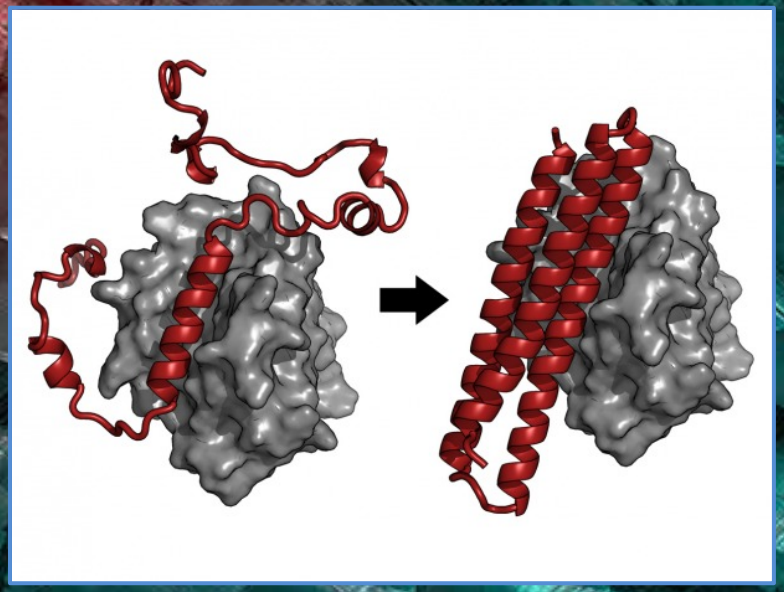
Oscillator

Sources of DNA

- Natural sequences and metabolic pathways

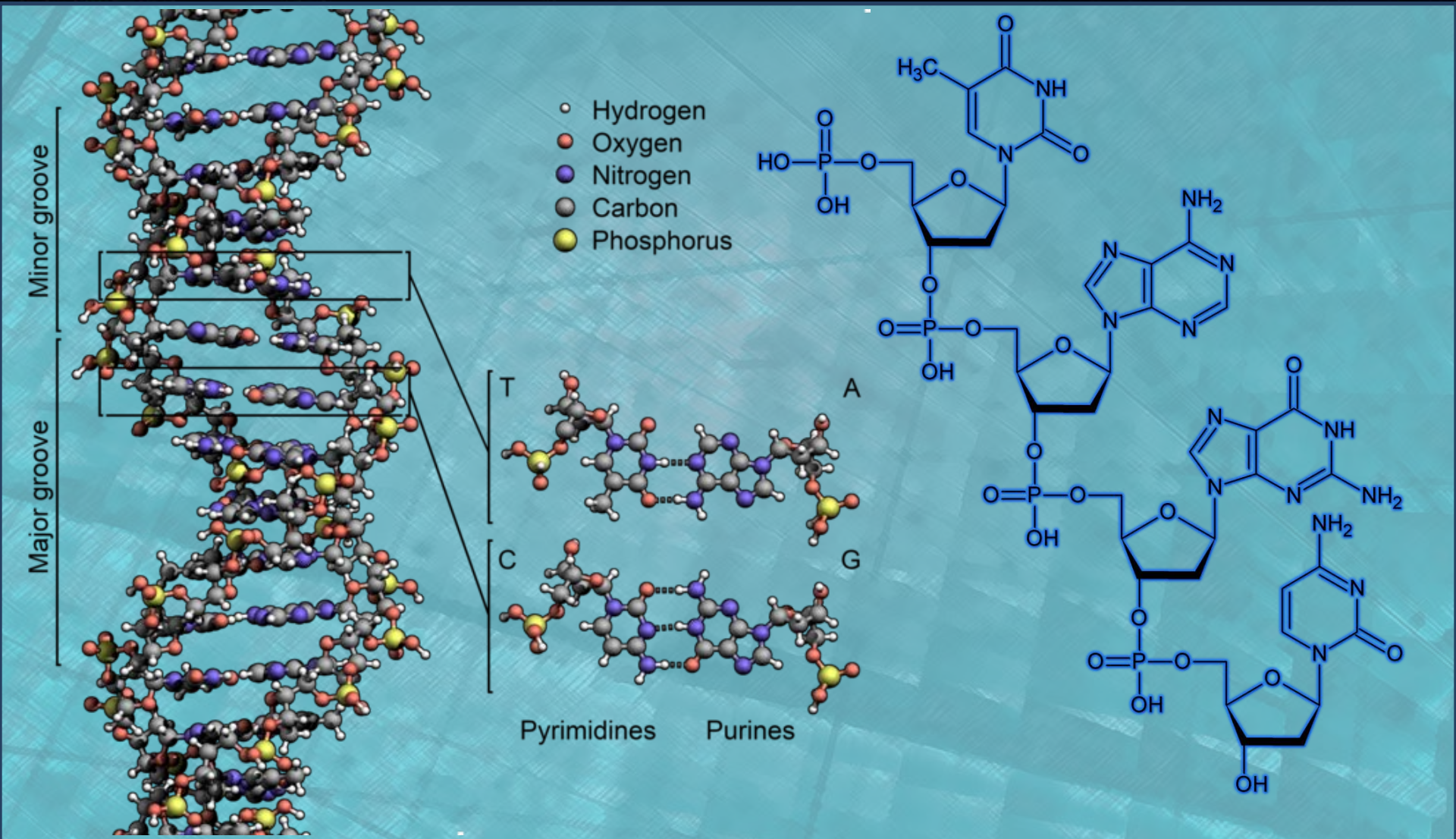


- Modified natural sequences

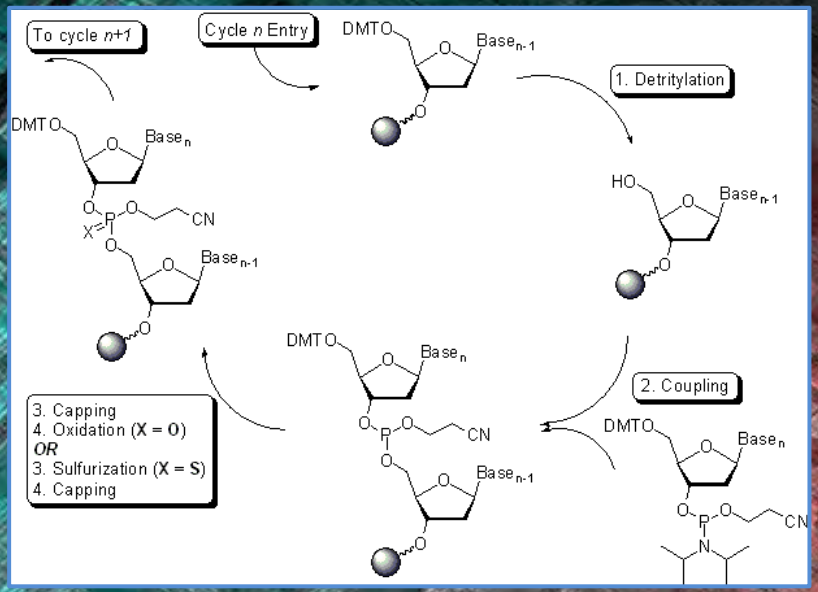


- Artificially created sequences

Structure of DNA

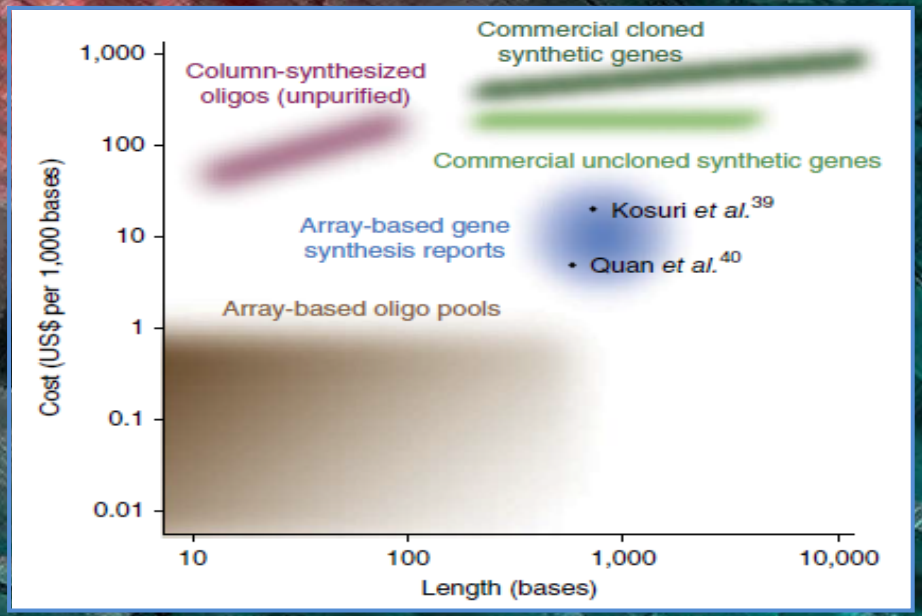


DNA synthesis



- Works fine for pieces shorter than 75 nt
- The maximum lenght of oligo which can be synthesised is 200

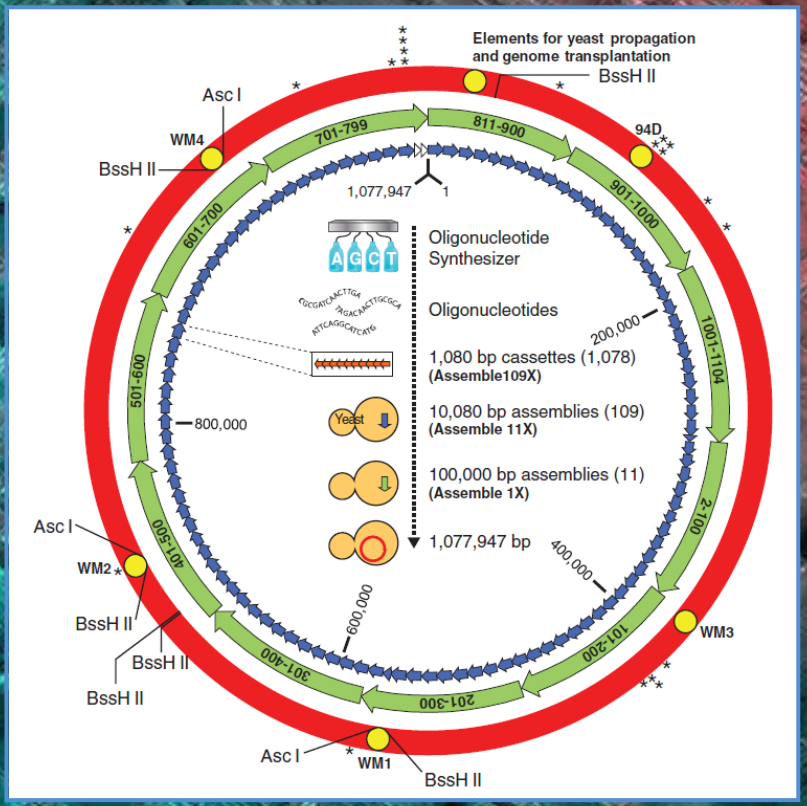
The chemistry was invented in 70' and it has not been changed since that

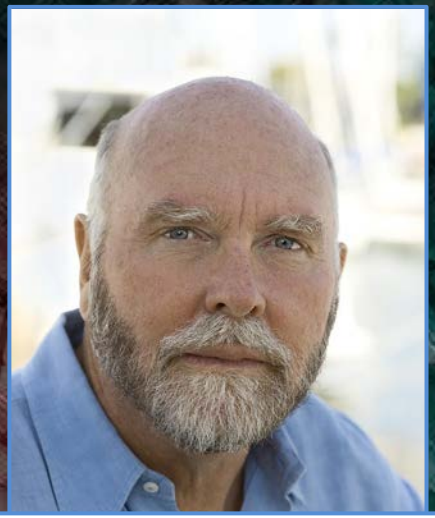


Synthetic genomes

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2]*



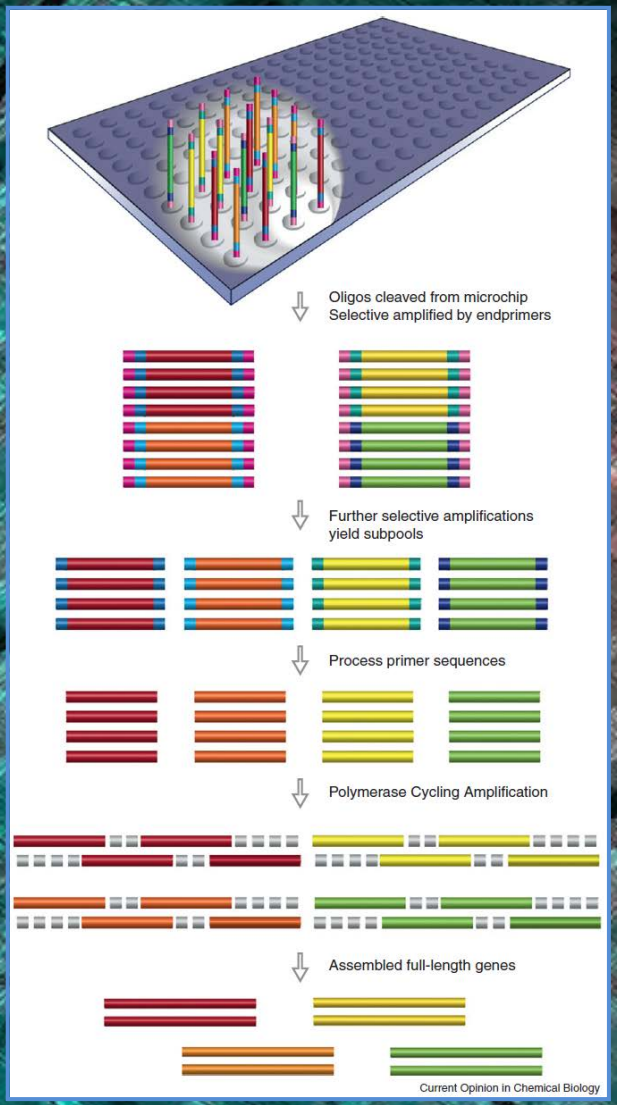


creator...

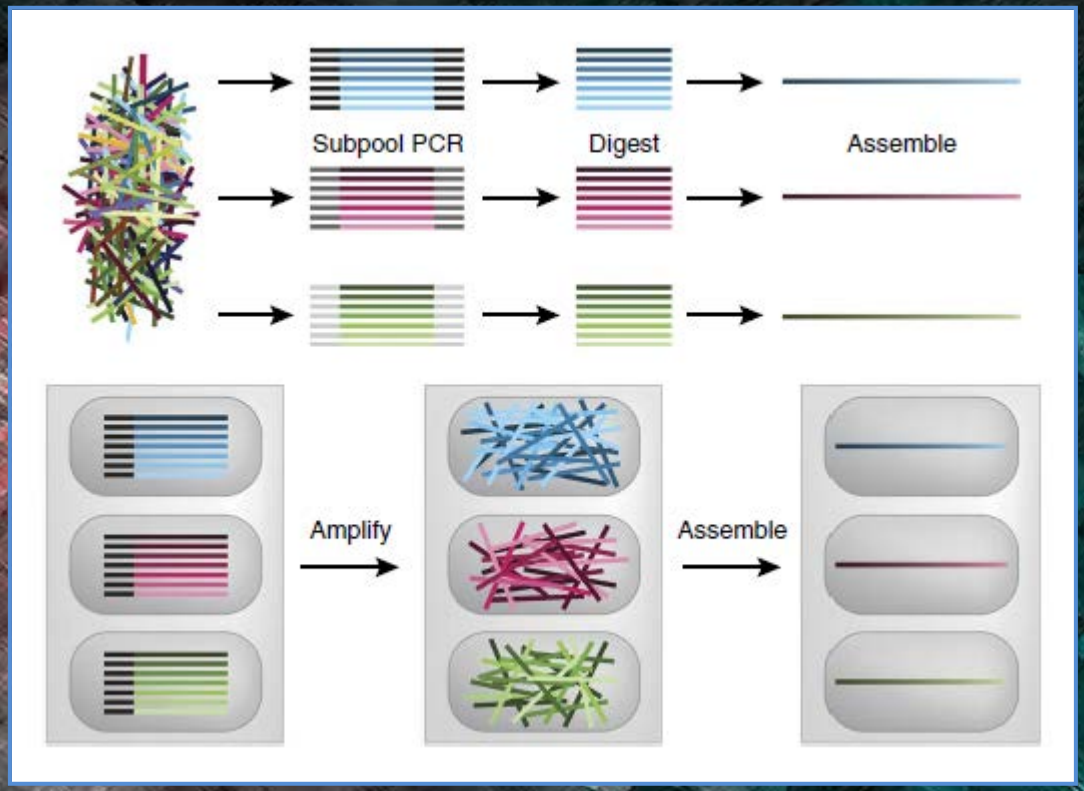
and its creation

Science **329, 52 (2010)**

Some novel methods of DNA synthesis

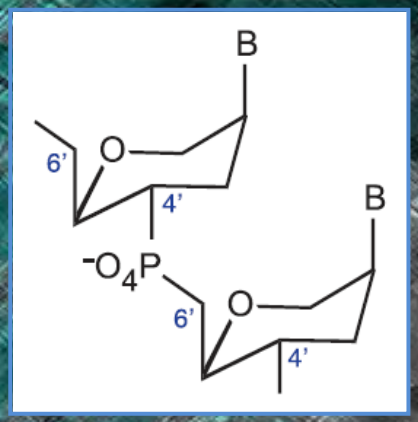


Current Opinion in Chemical Biology 2012, 16:260–267

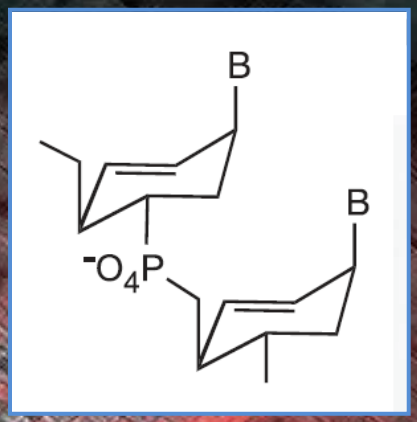


nature methods | VOL.11 NO.5 | MAY 2014

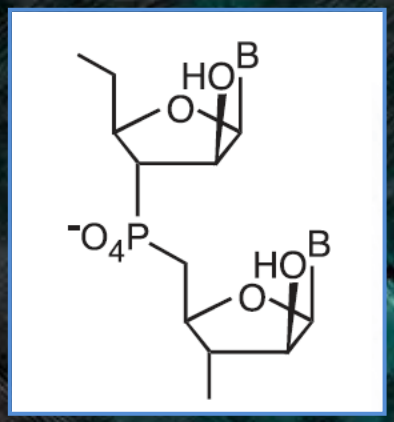
Xeno Nucleic Acids



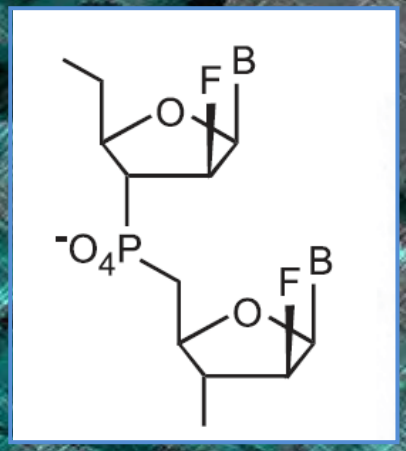
HNA
(1,5-anhydrohexitol nucleic acid)



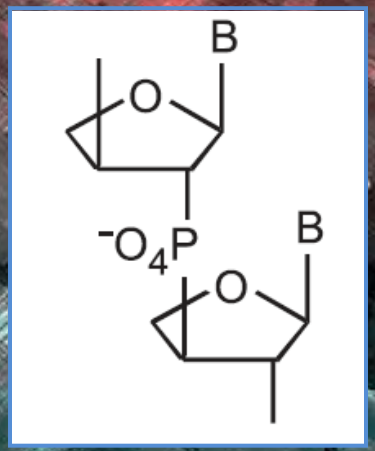
CeNA
(cyclohexenyl nucleic acid)



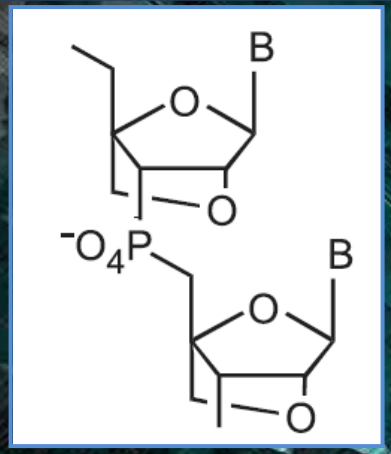
ANA
(arabinonucleic acid)



FANA
(2' fluoro-arabinonucleic acid)



TNA
(α-L-threofuranosyl nucleic acid)



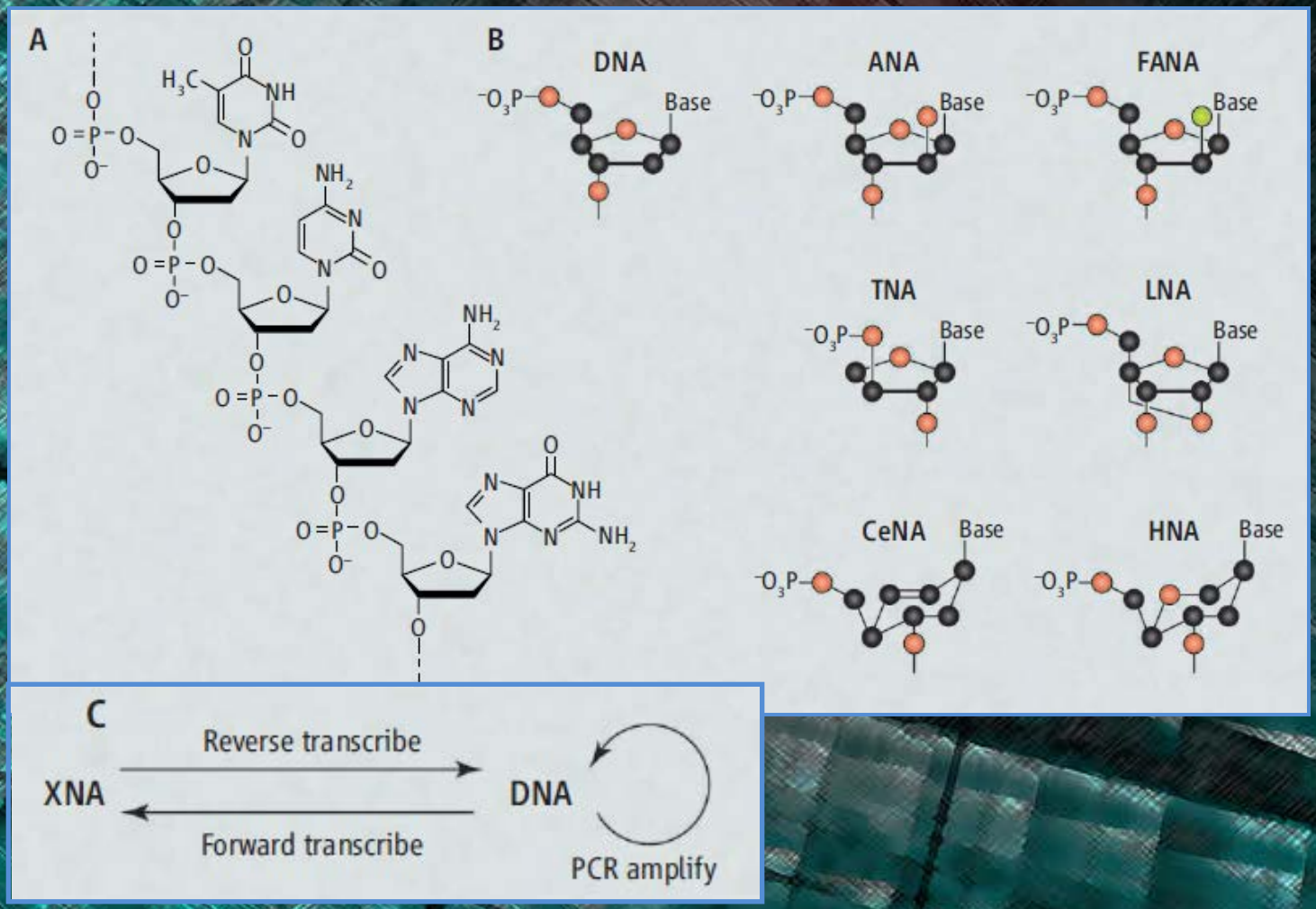
LNA
(locked nucleic acid)

Synthetic Genetic Polymers Capable of Heredity and Evolution

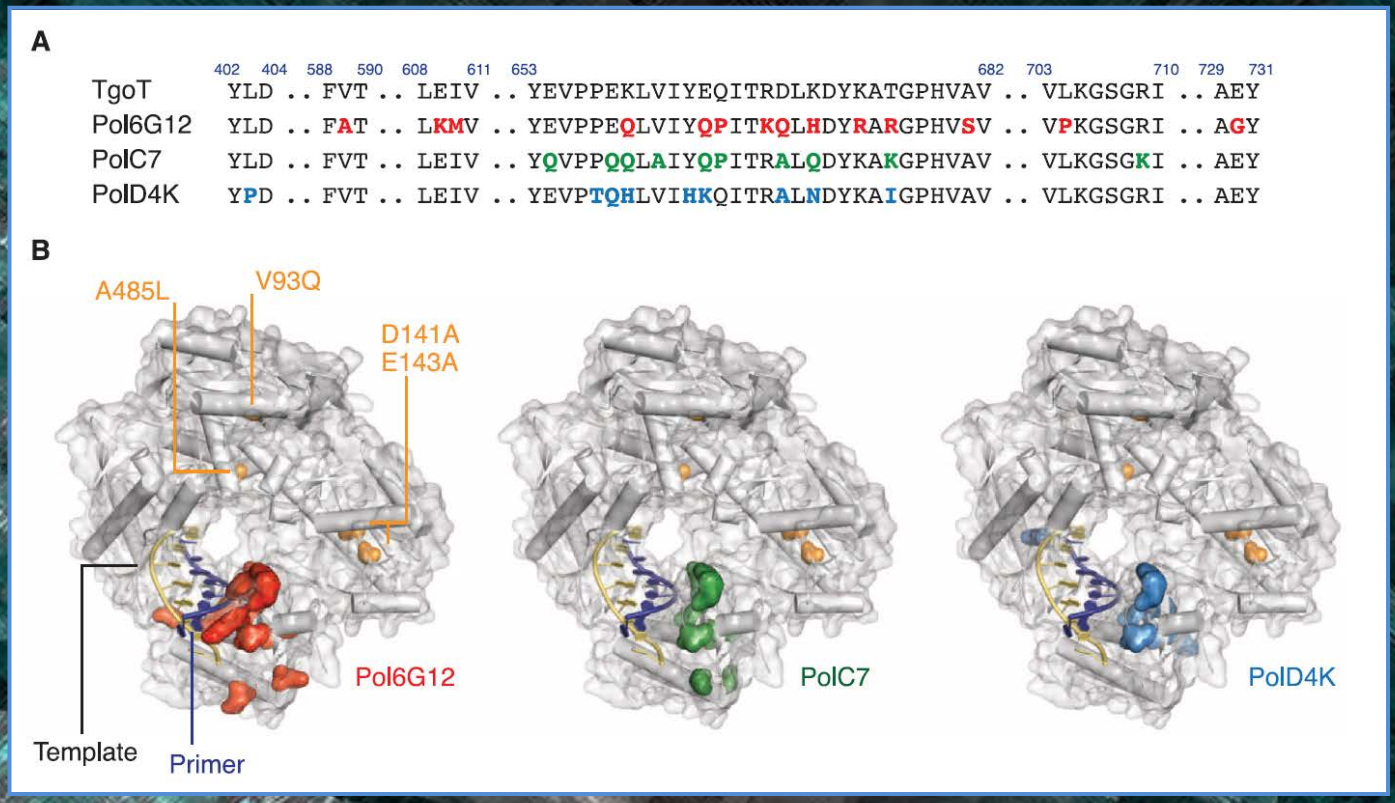
Vitor B. Pinheiro,[1] Alexander I. Taylor,[1] Christopher Cozens,[1] Mikhail Abramov,[2] Marleen Renders,[2*] Su Zhang,[3] John C. Chaput,[3] Jesper Wengel,[4] Sew-Yeu Peak-Chew,[1] Stephen H. McLaughlin,[1] Piet Herdewijn,[2] Philipp Holliger[1]†

Science

AAAS



Polymerases recognising XNAs



(A) Sequence alignments showing mutations from Tgo consensus in polymerases Pol6G12 (red), PolC7 (green), and PolD4K (blue).

(B) Mutations are mapped on the structure of Pfu (Protein Data Bankidentification code: 4AIL). Yellow, template; dark blue, primer; orange, mutations present in the parent polymerase TgoT.

Paradigm shift - bioorthogonality

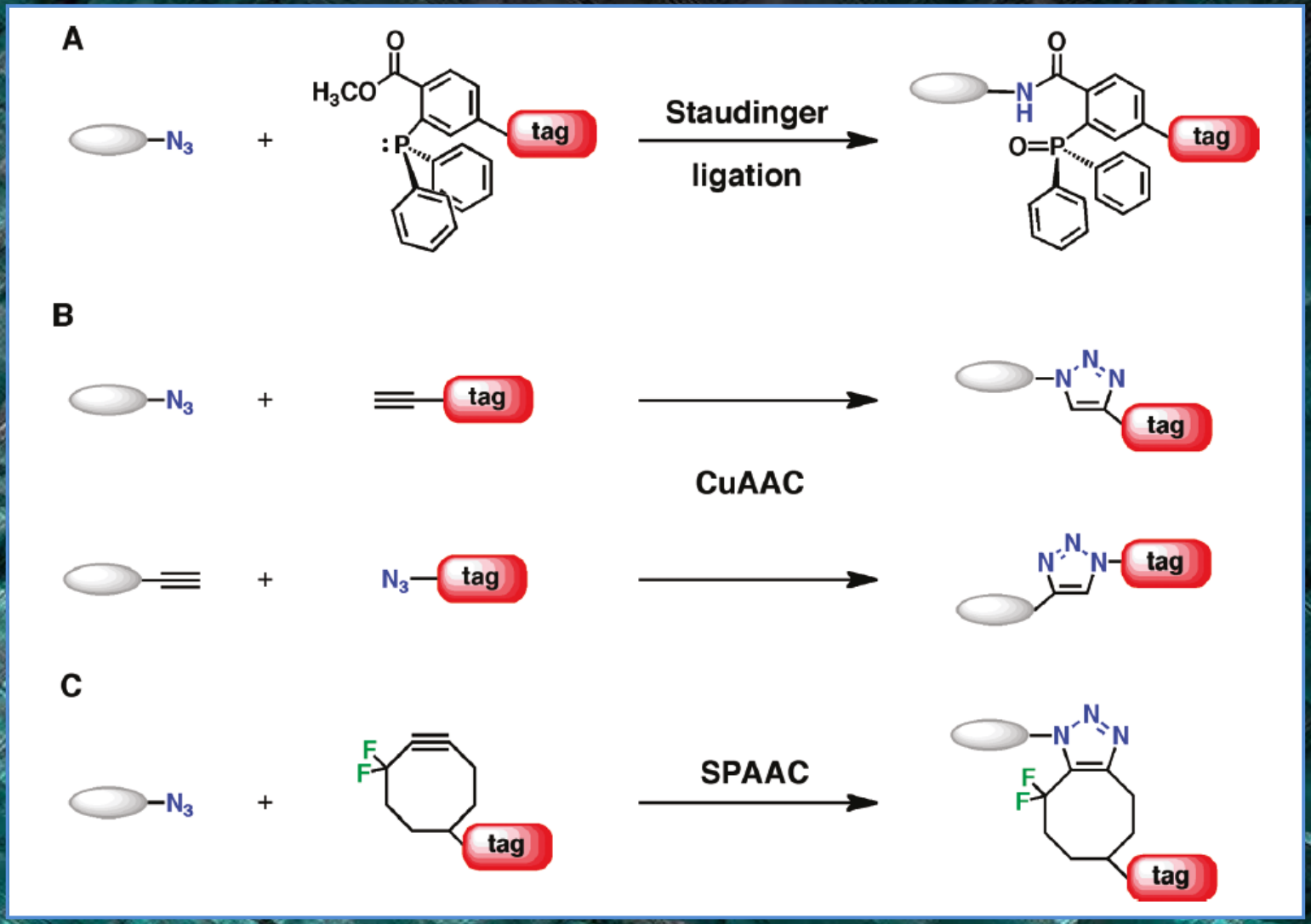
"molecular details of biological processes can be most accurately understood by probing biomolecules within their native habitats, that is, in cells, or even better, live organisms"

Carolyn R. Bertozzi

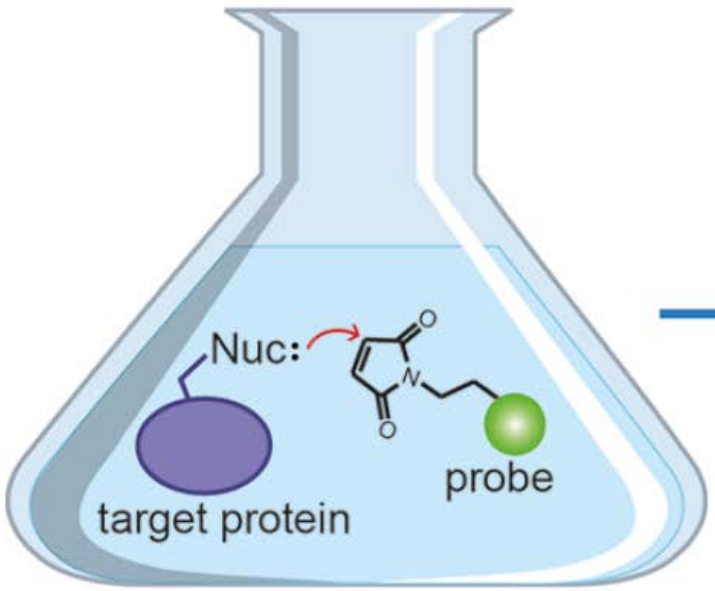
"A bioorthogonal reaction typically requires the two participating components (bioorthogonal reaction pair) to be mutually reactive while remaining inert to the surrounding molecules under the physiological environment"

ACCOUNTS OF CHEMICAL RESEARCH; 742–751; 2011; Vol. 44; No. 9

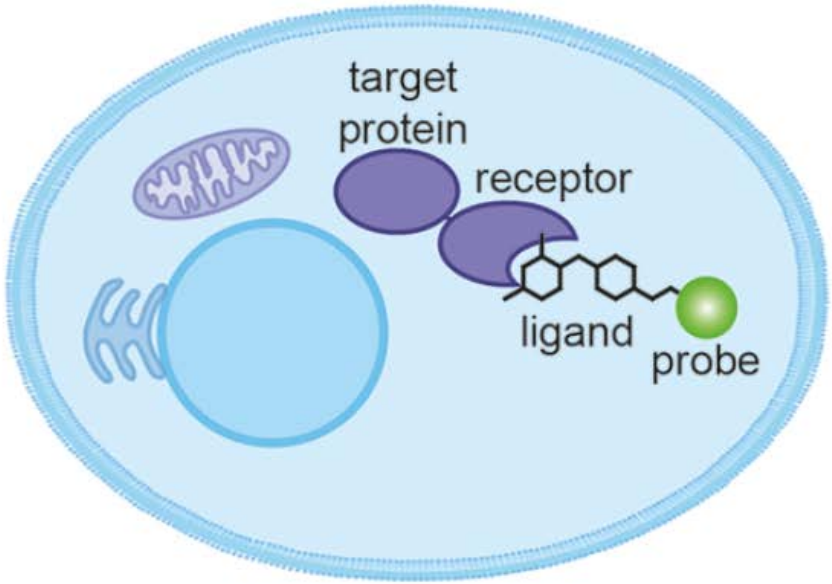
Some methods working *in vivo*



New ideas in molecular tagging



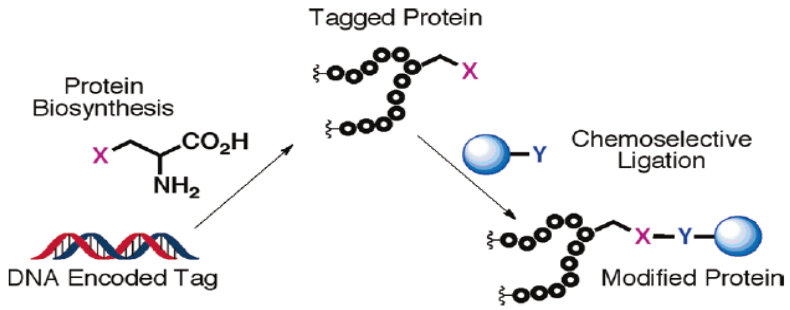
20th century - labeling purified proteins in test tubes

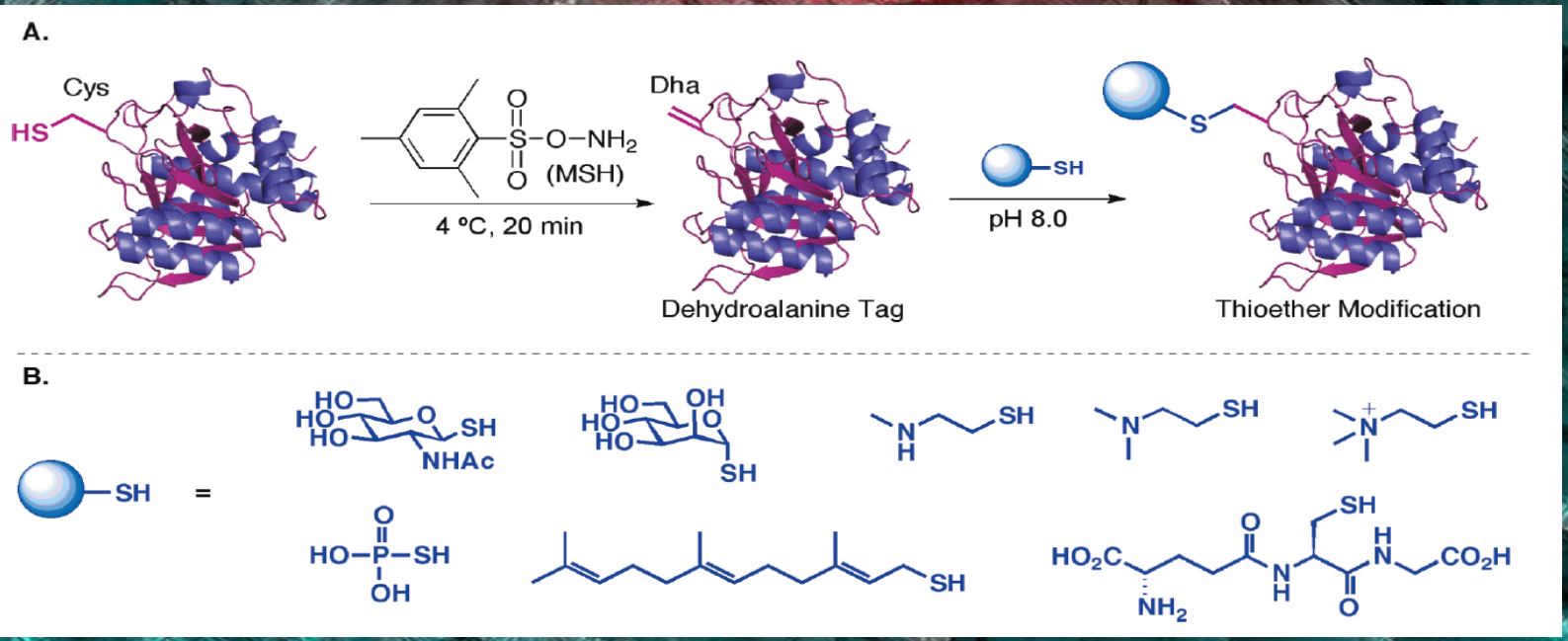


21st century - labeling proteins in the complex environment of live cells

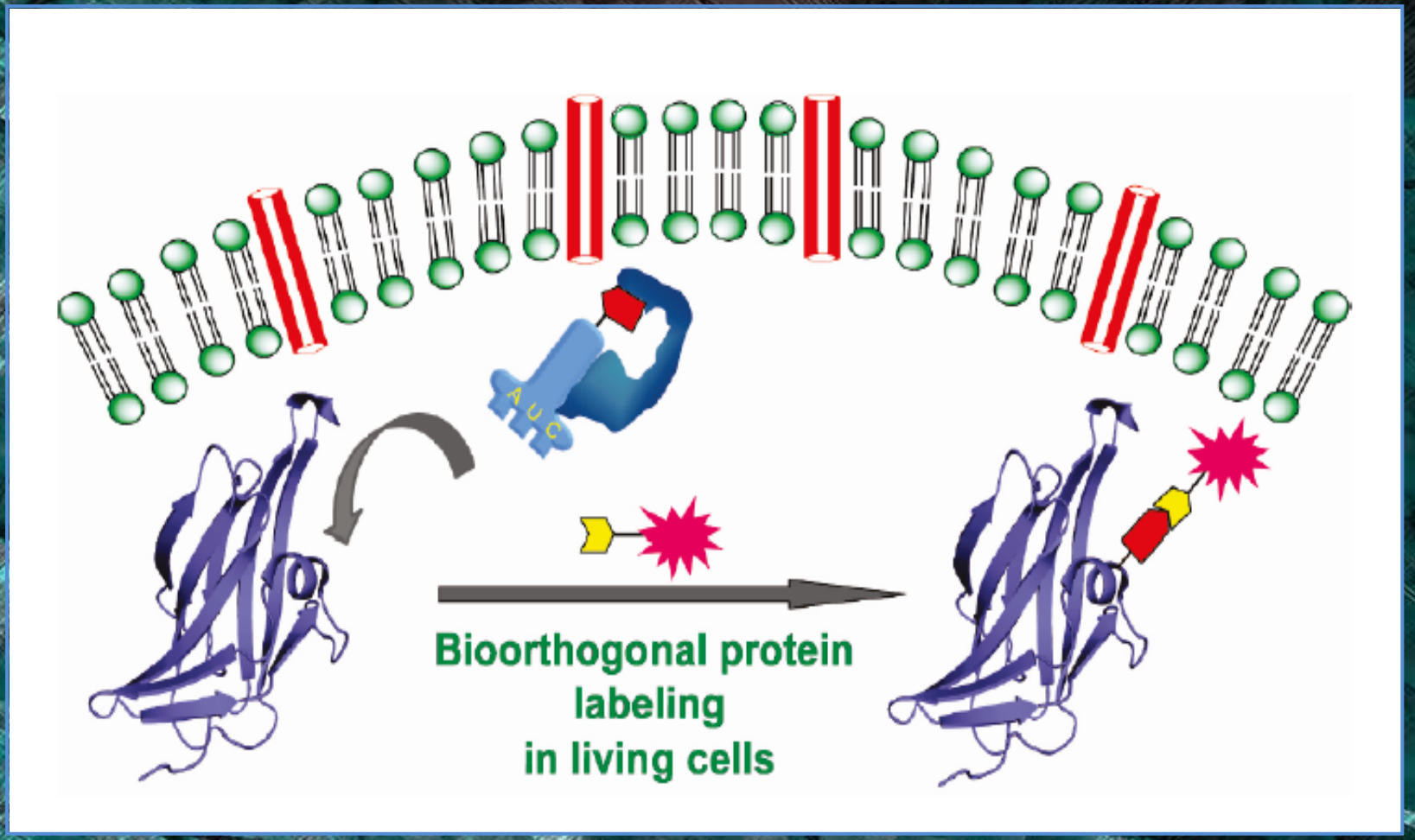
Protein modifications

SCHEME 1. A Tag-and-Modify Strategy for Site-Selective Protein Modification

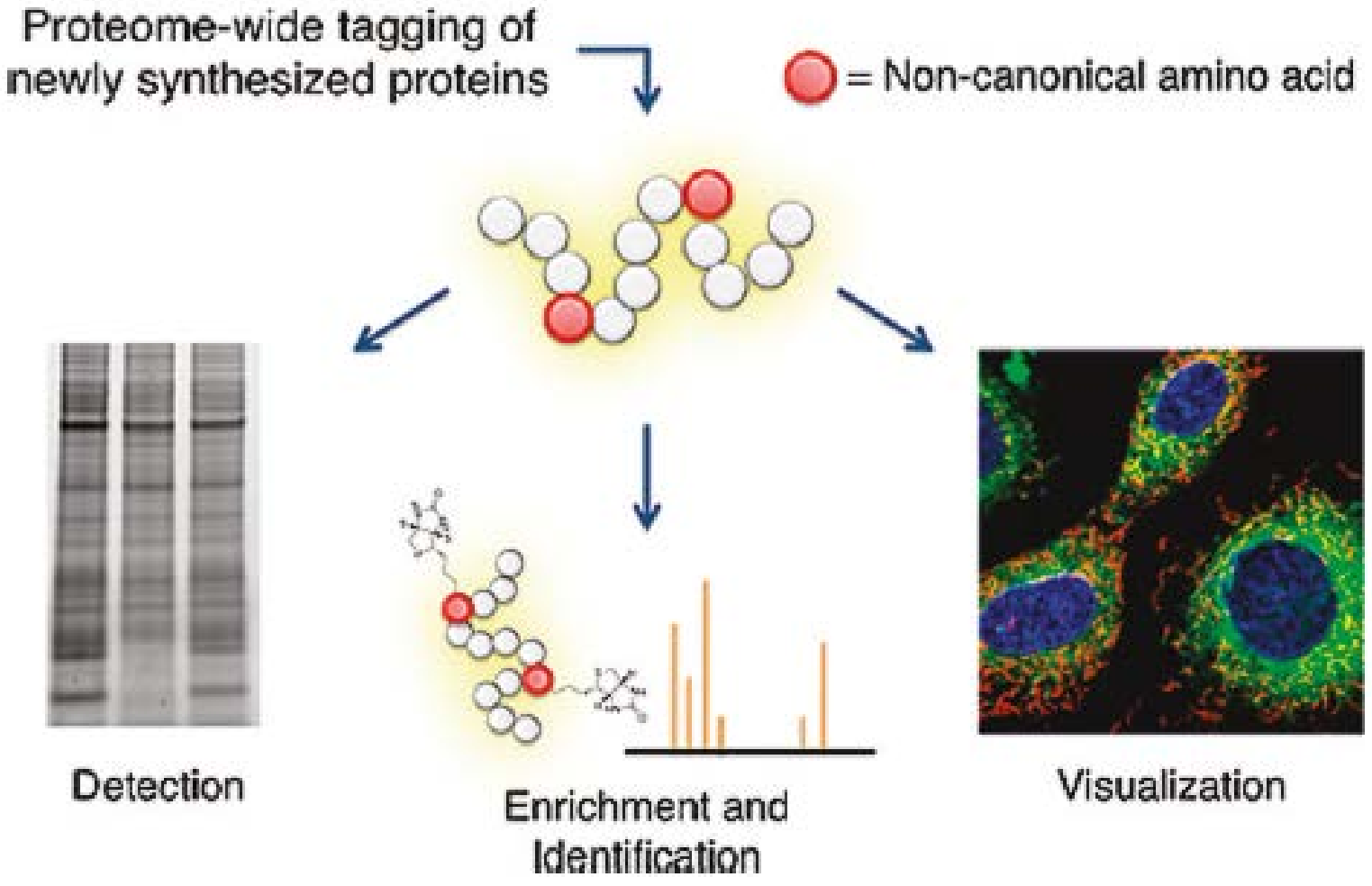




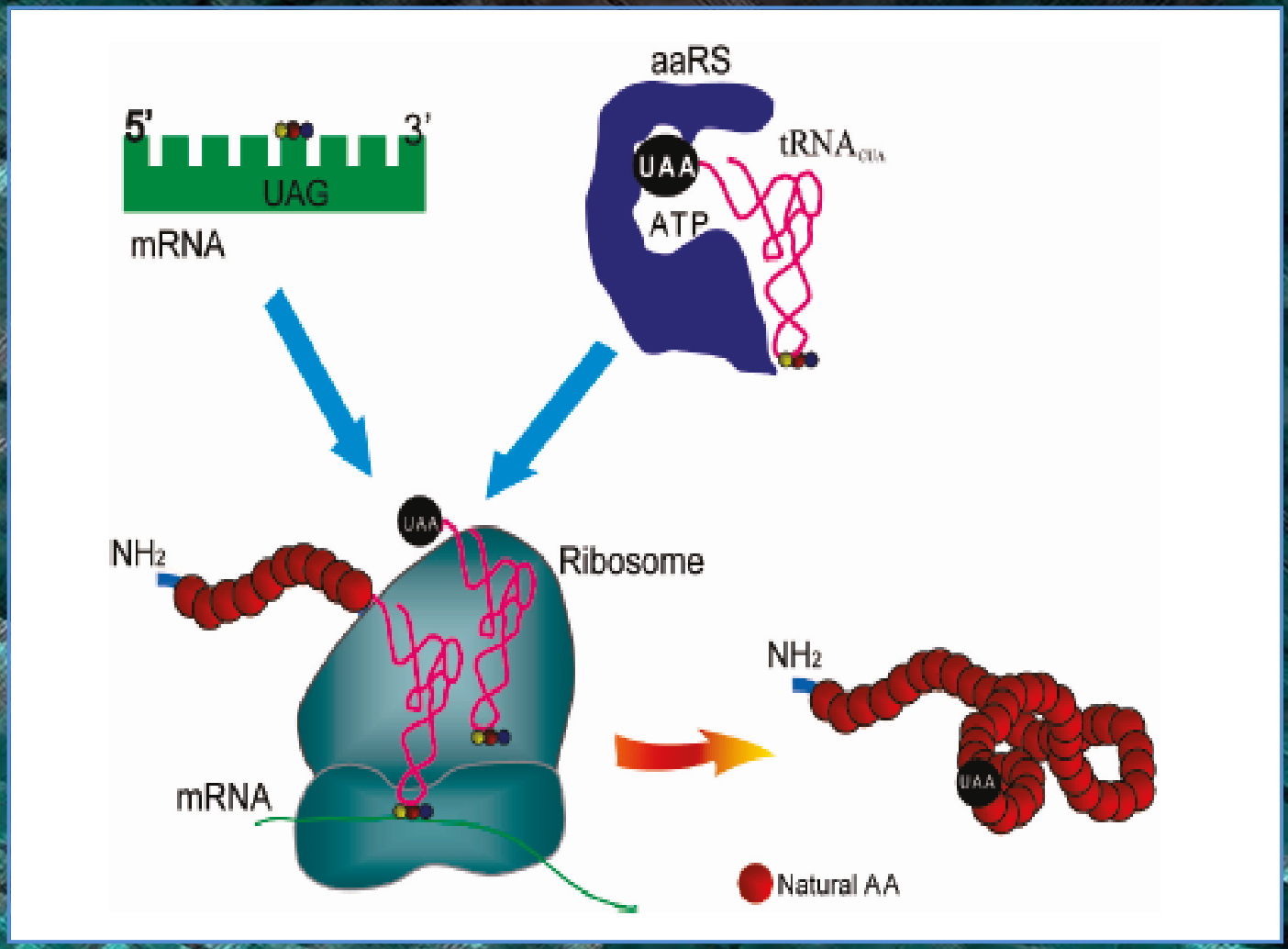
Protein alterations *in vivo*



Residue specific incorporation

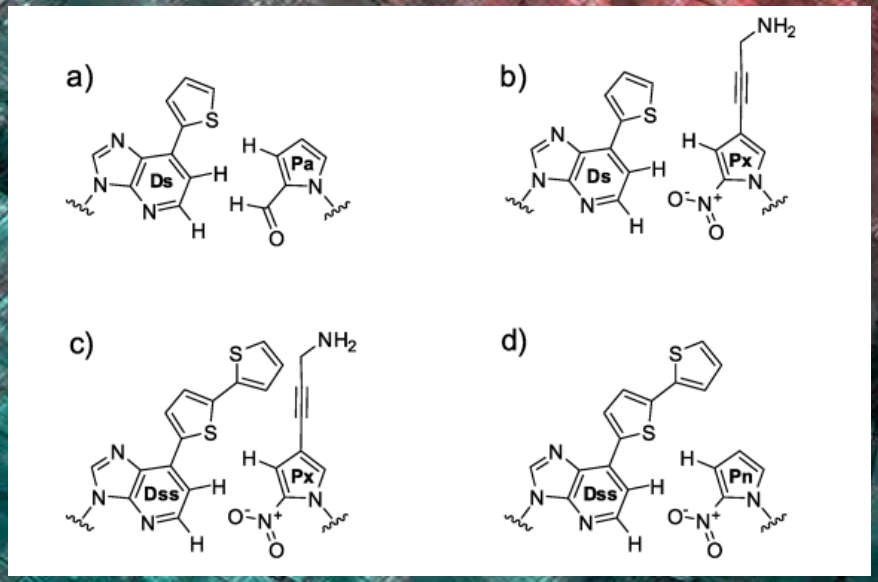


Site specific incorporation

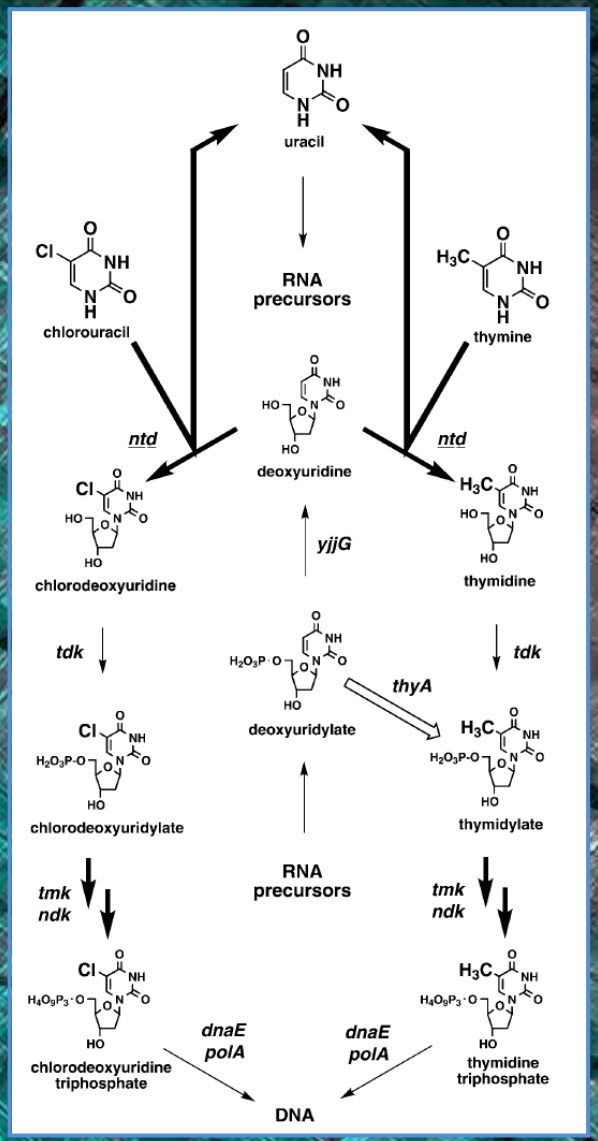


New emerging field - xenobiology

- It is not about searching extraterrestial life (this is called astrobiology)
- It is about investigating the possibility of life based on altered biochemistry (different proteins, nucleic acids etc)



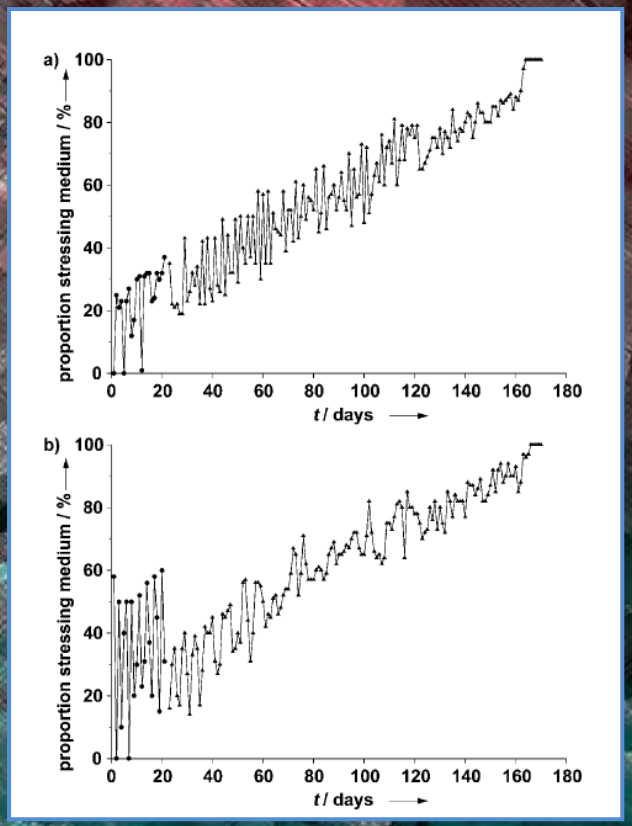
Chemistry and Biology - combined effort



Chemically Modified Organisms

Chemical Evolution of a Bacterium's Genome**

*Philippe Marlière, Julien Patrouix, Volker Döring, Piet Herdewijn, Sabine Tricot, Stéphane Cruveiller, Madeleine Bouzon, and Rupert Mutzel**



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Thank you for listening