spontaneous generation of genetic polymers

Ernesto Di Mauro Università di Roma “Sapienza”

or … ab initio nanotechnology

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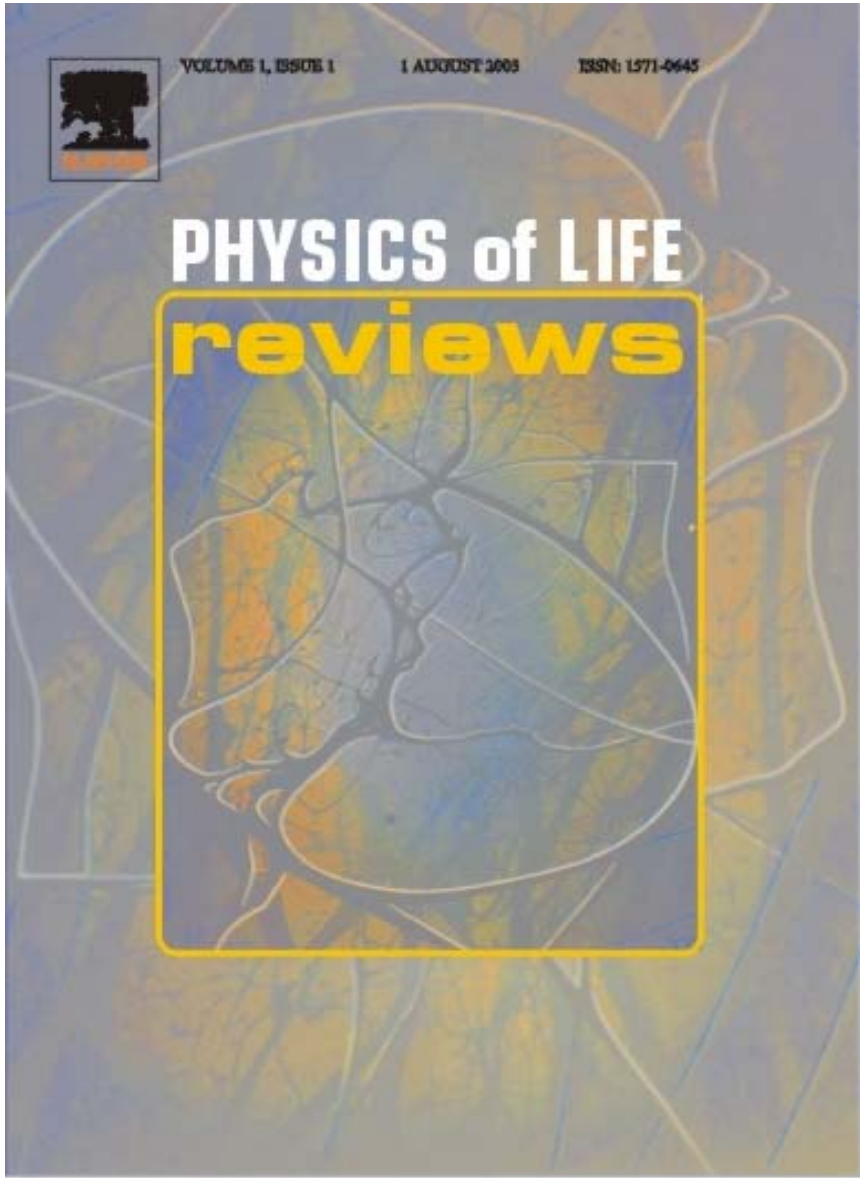

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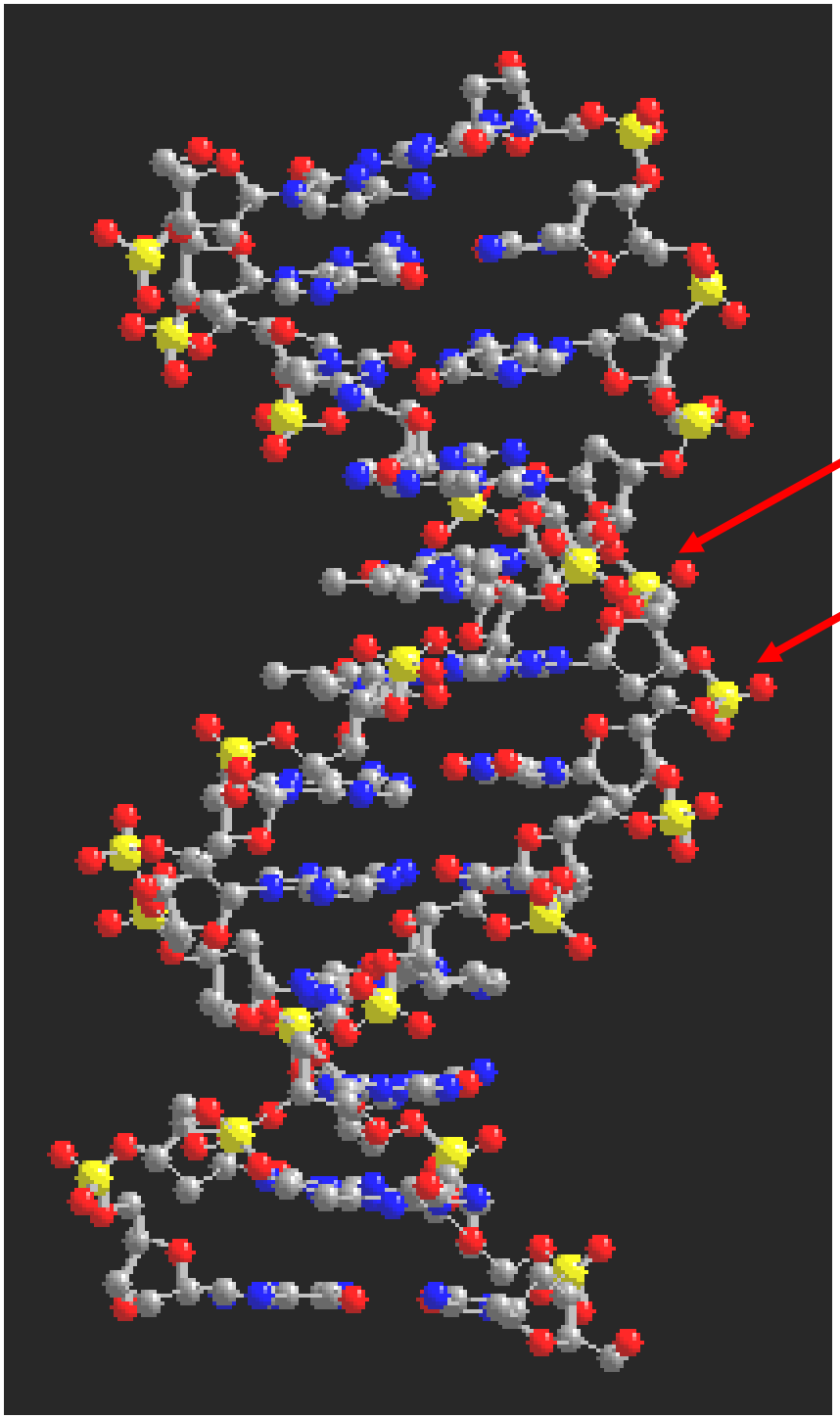
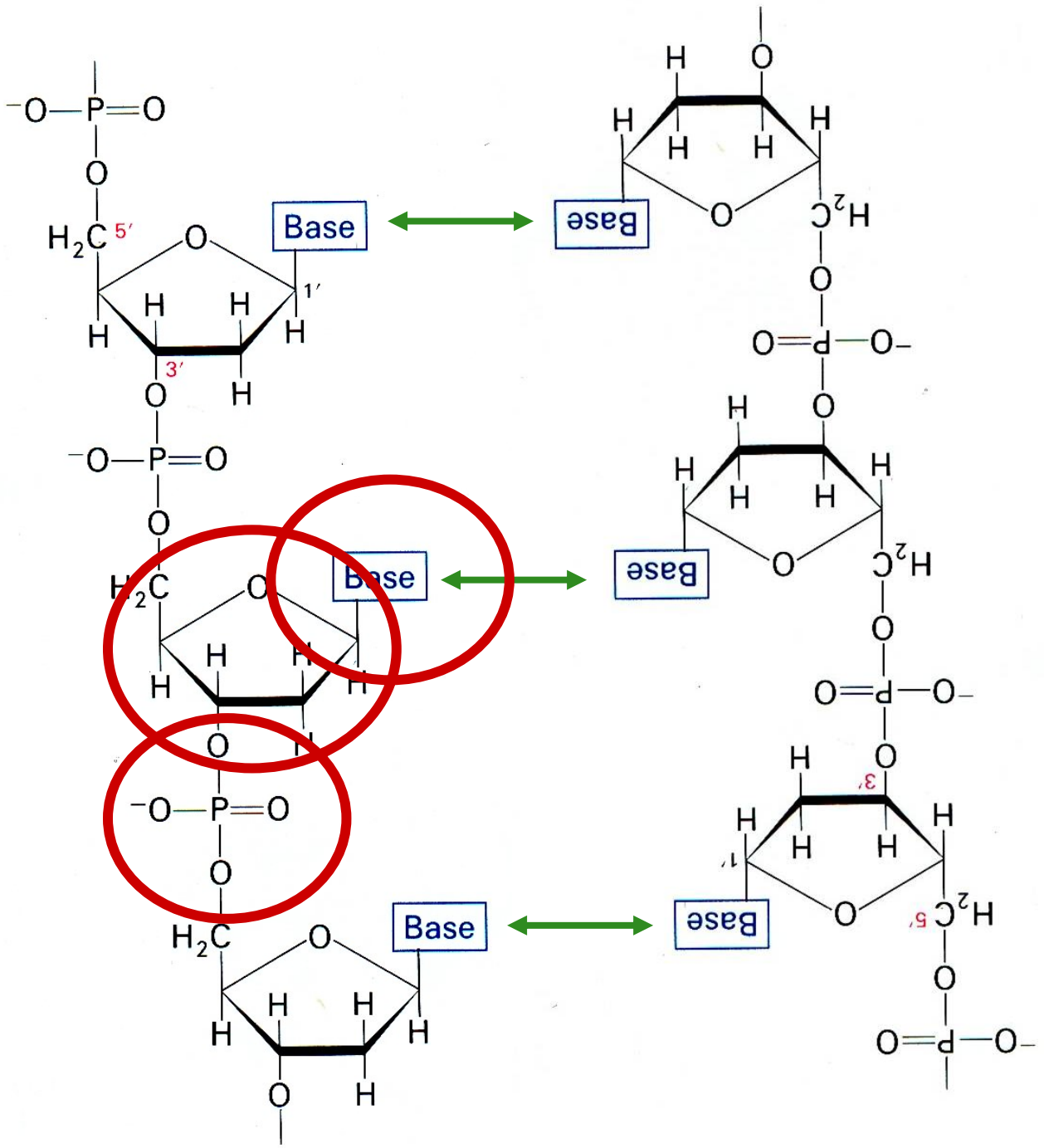



Base
Base
Base
Base
Base
Base

atomic transformations

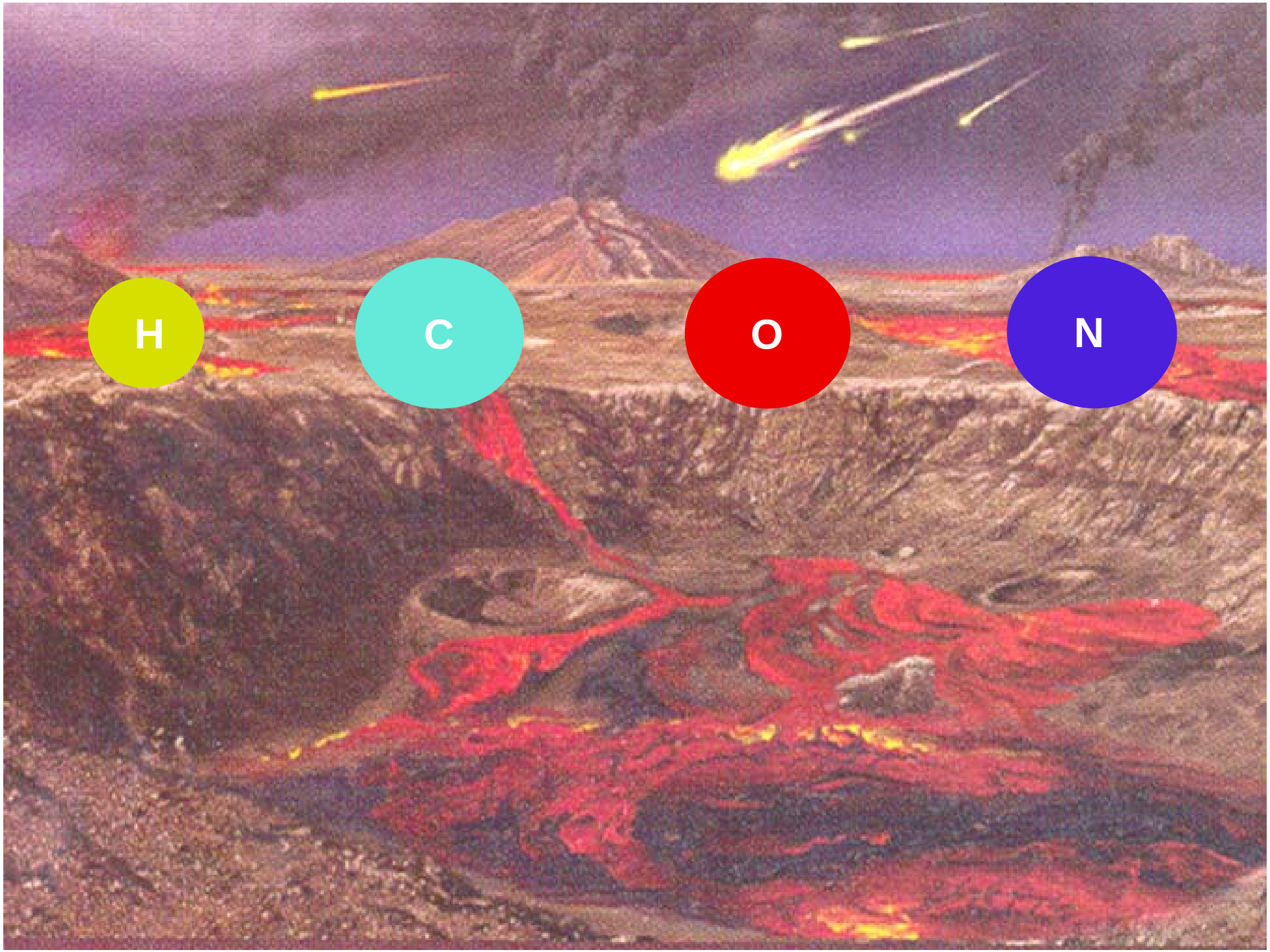
$$3\ {}^{4}He \longrightarrow {}^{12}C$$

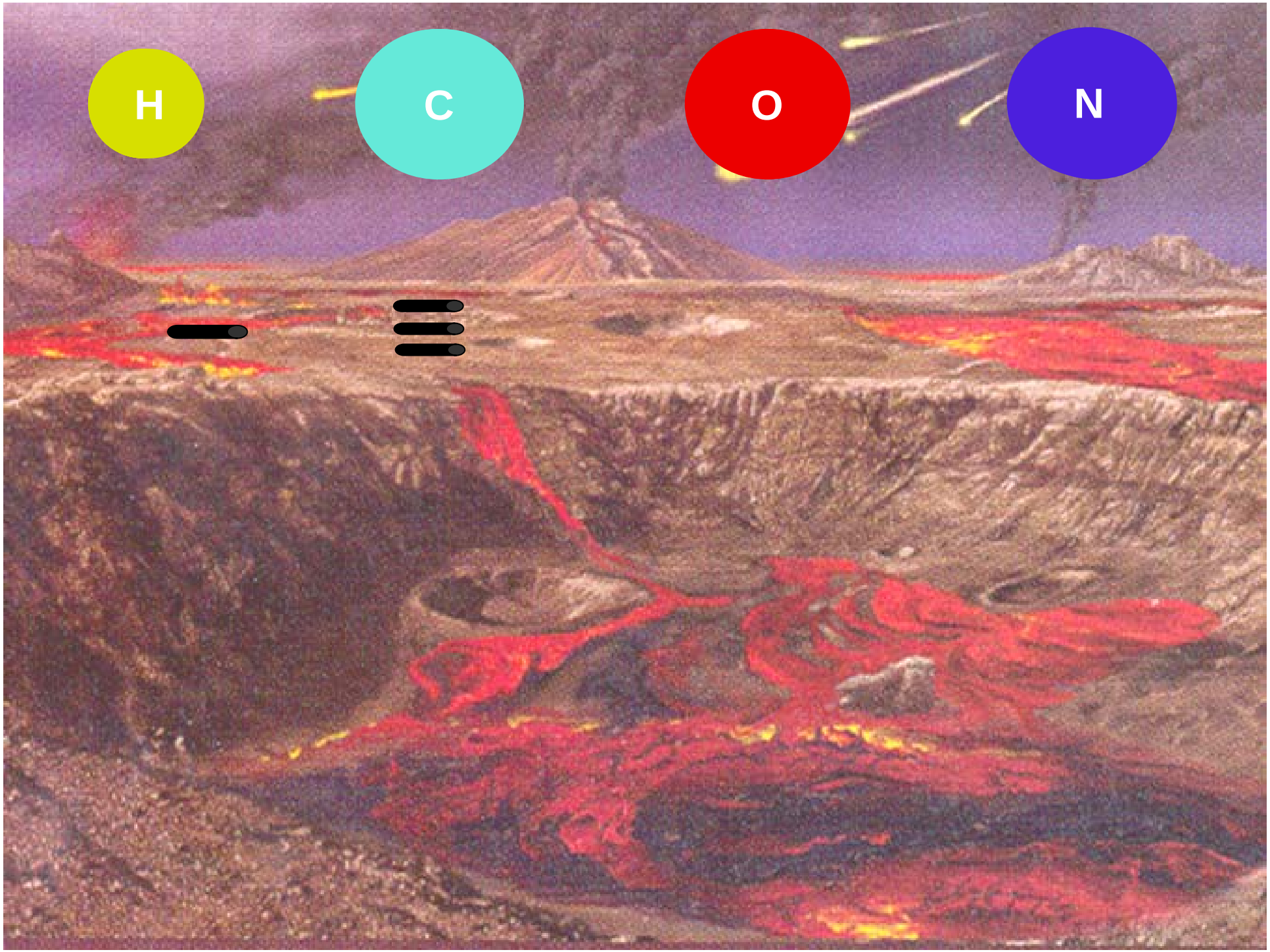
$${}^{12}C + {}^{4}He \longrightarrow {}^{16}O$$

$${}^{16}O + {}^{16}O \longrightarrow {}^{31}P + {}^{1}H$$

$${}^{1}H \xrightarrow[CNO]{CN} {}^{4}He + \text{N secondary product}$$

$$8\ {}^{4}He \longrightarrow {}^{32}S$$


H
C
O
N


H
C
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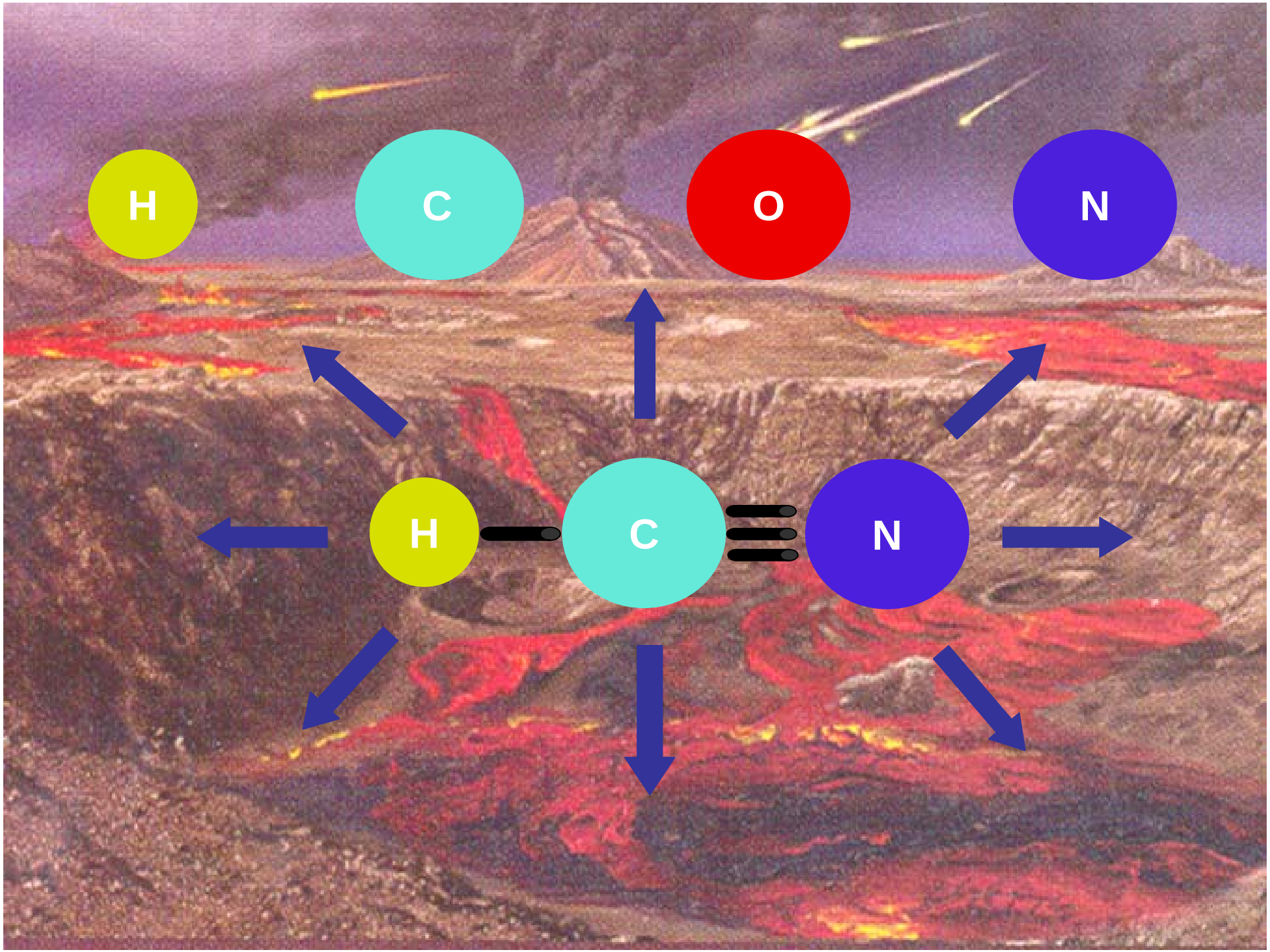
H
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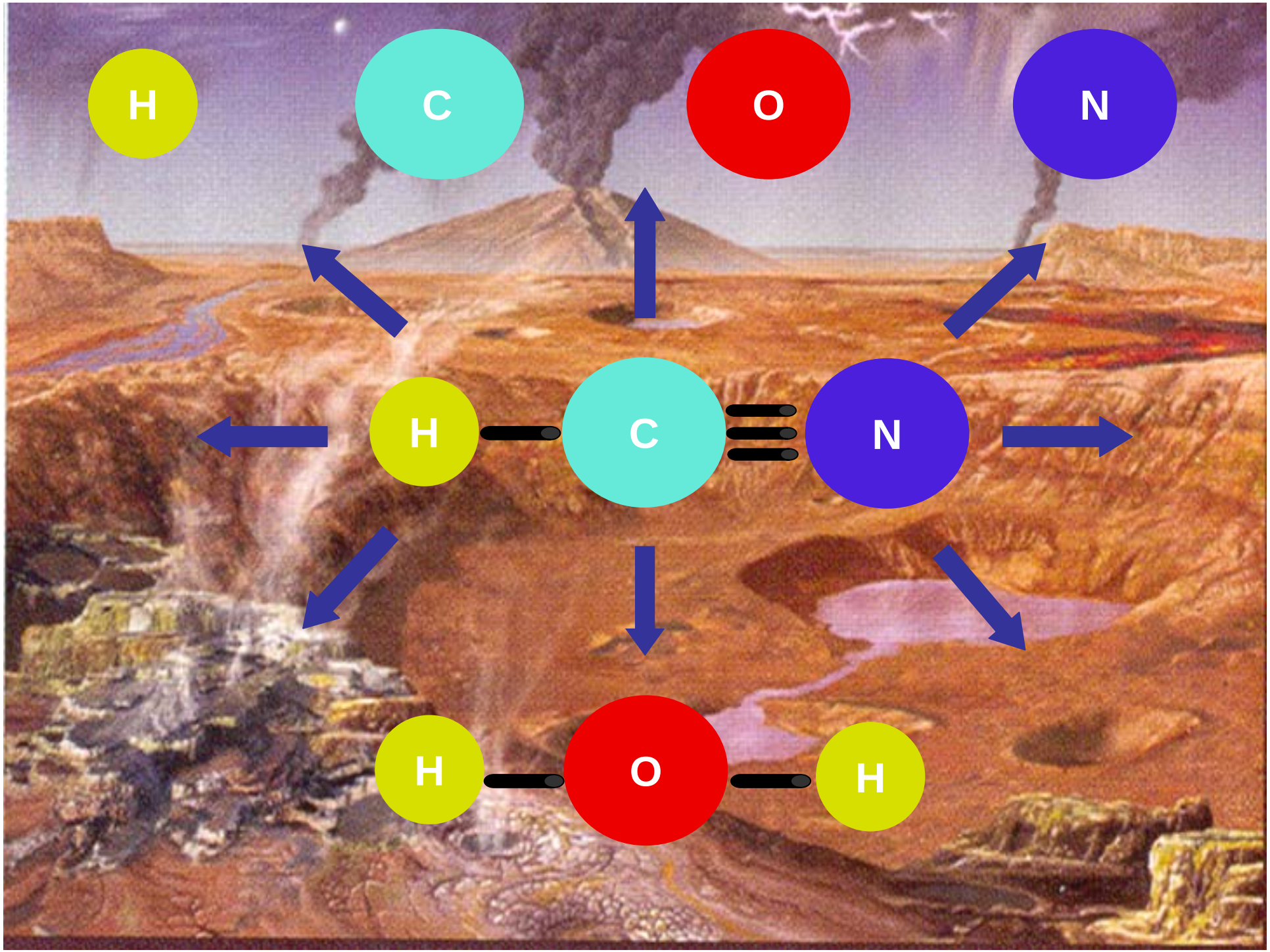
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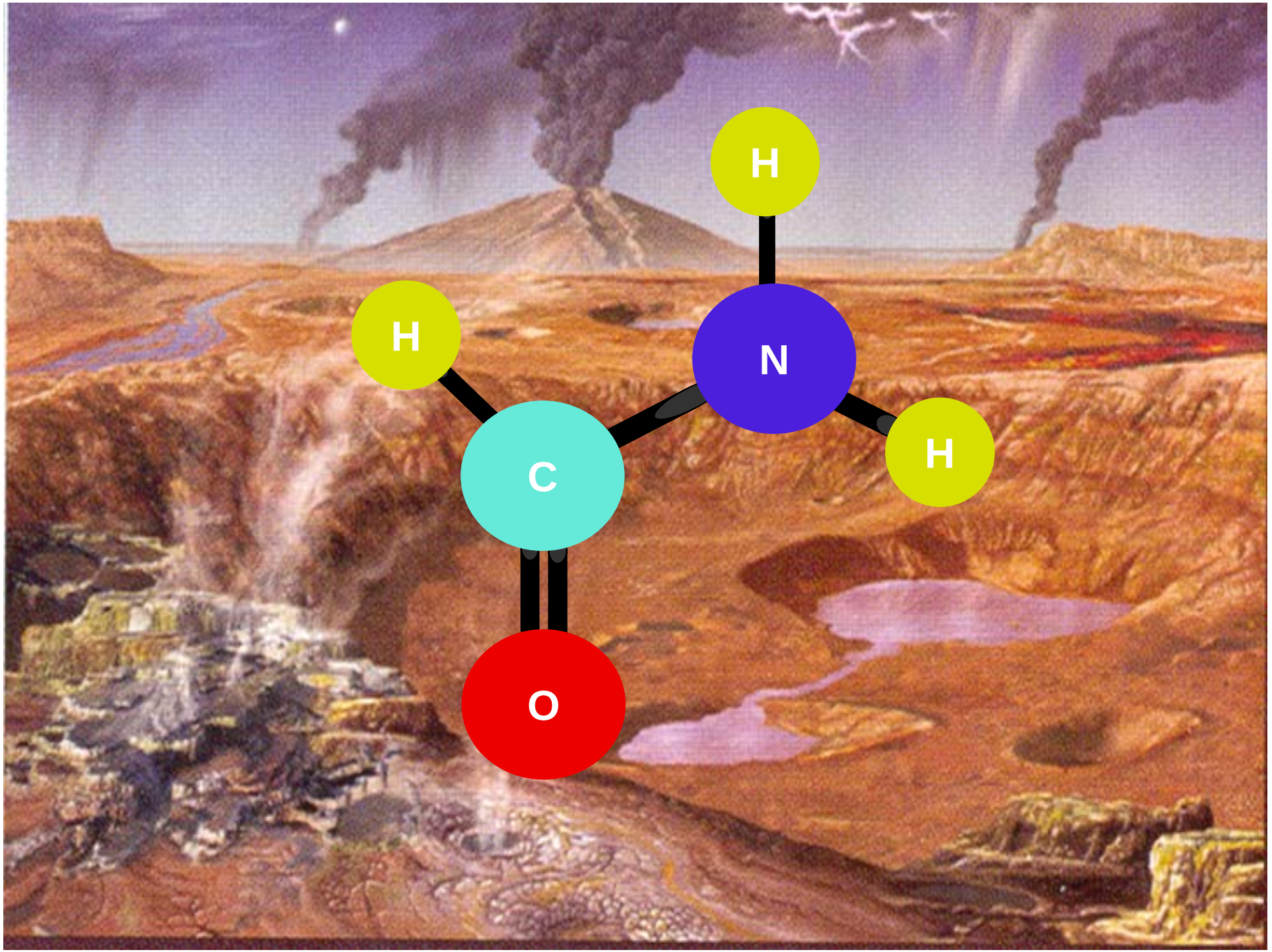
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H
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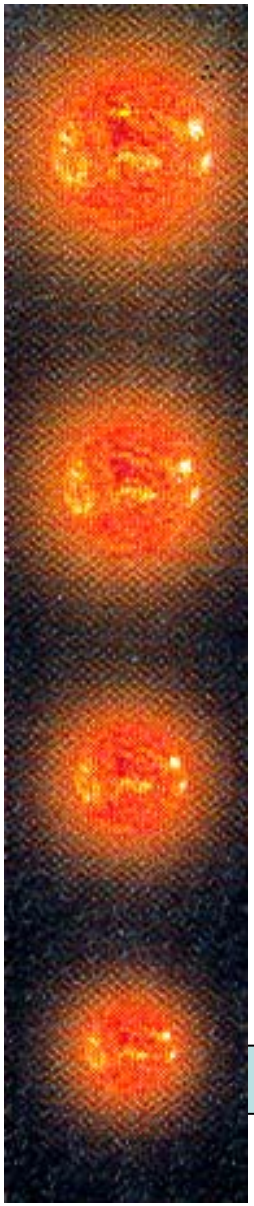
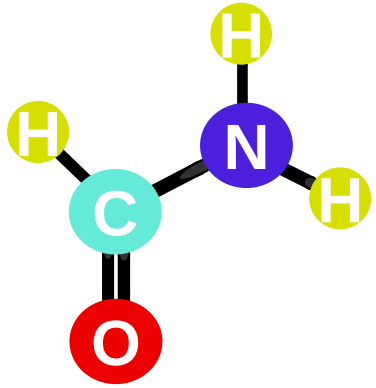
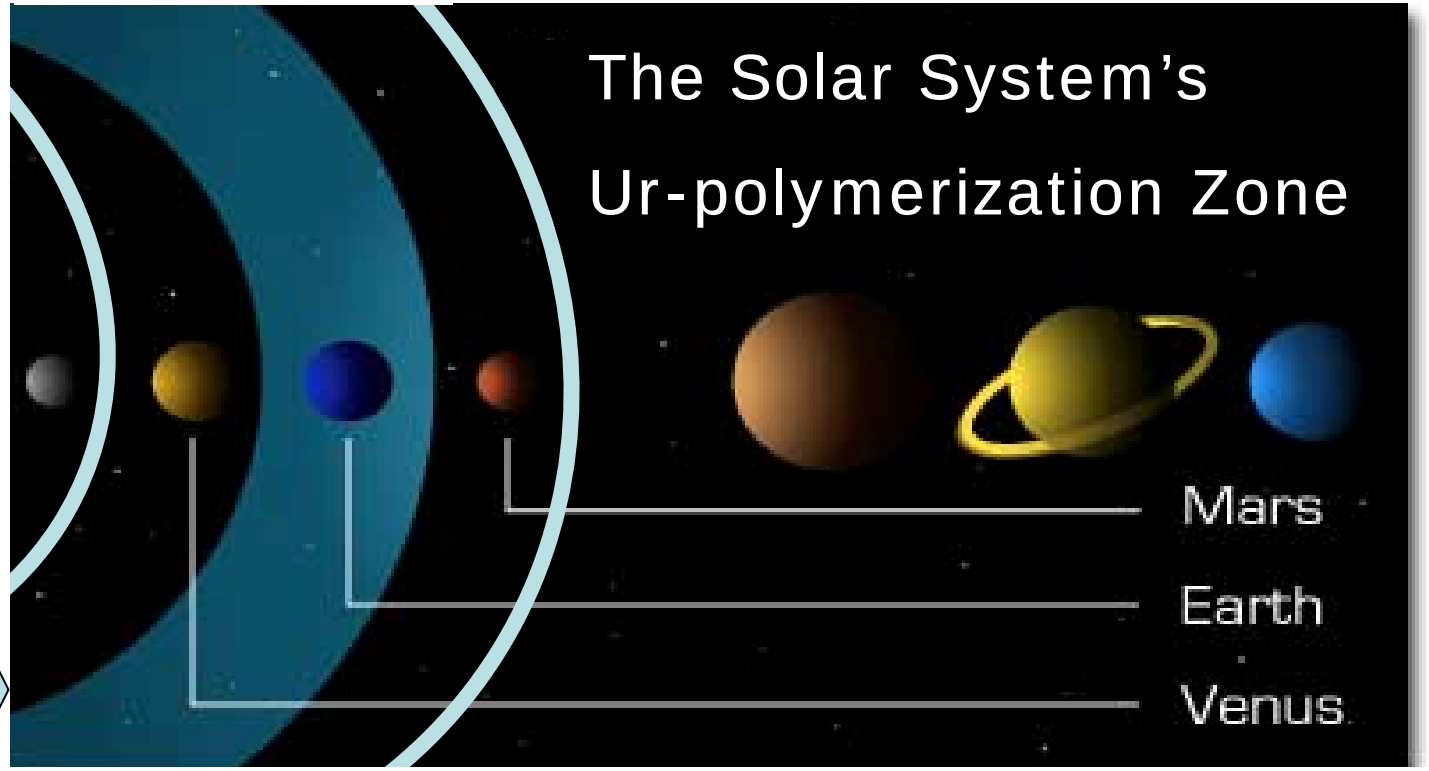
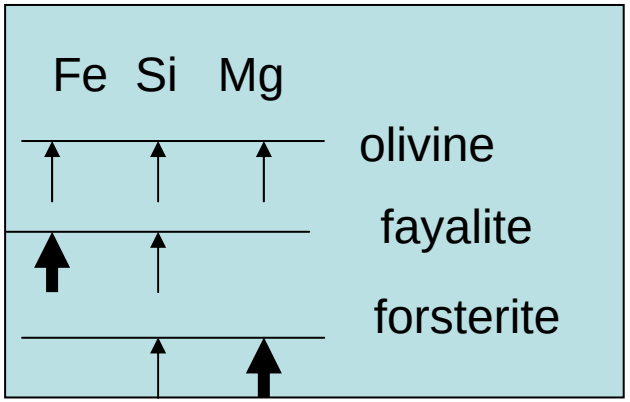




liquid between 4 and 210°C



- **circumstellar/cometal dusts** — silicates [(Mg,Si,Fe)O]



- **clays**

zeolites (Al,Ca,Na silicates)
kaolin
montmorillonites (μcrystalline phyllosilicates)
$(Na,Ca)\ (Al, Mg)_6\ (Si_4O_{10})_3\ (OH)_6.nH_2O$

- **metal oxides** — (impact-induced minerals)

CaO MnO_2 SiO
MgO Al_2O_3 SiO_2
FeO
CuO

- **carbonates**

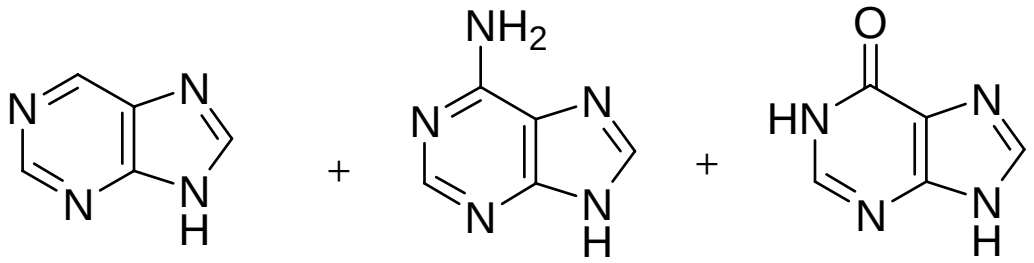
- **volcanism-related minerals**

perovskite ($CaTiO_3$)
TiO_2

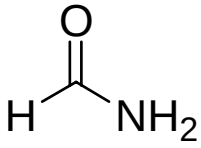
- **phosphates**

phosphate minerals

Catalytic Purine and Pyrimidine ring Formation From Formamide



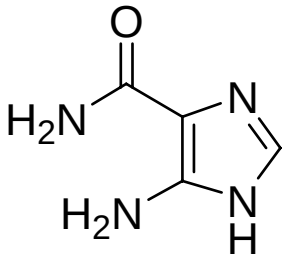
Purine **2** + Adenine **3** + Hypoxanthine **4**



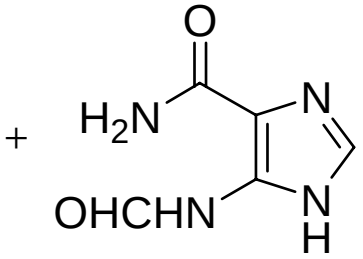
1

Montmorillonite*
(2%, w/w)

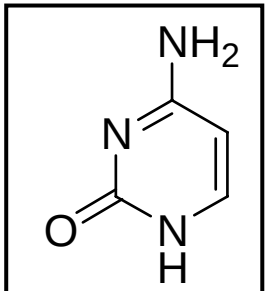
160°C, 48h



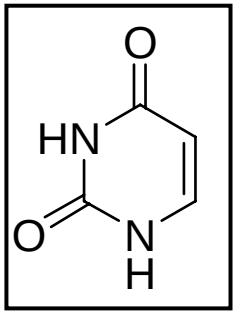
Aminoimidazole carboxamide (AICA) **5**



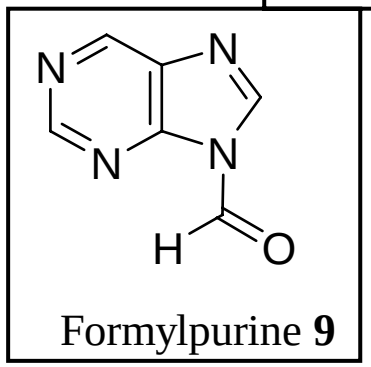
5-Form-AICA **6**



Cytosine **7**



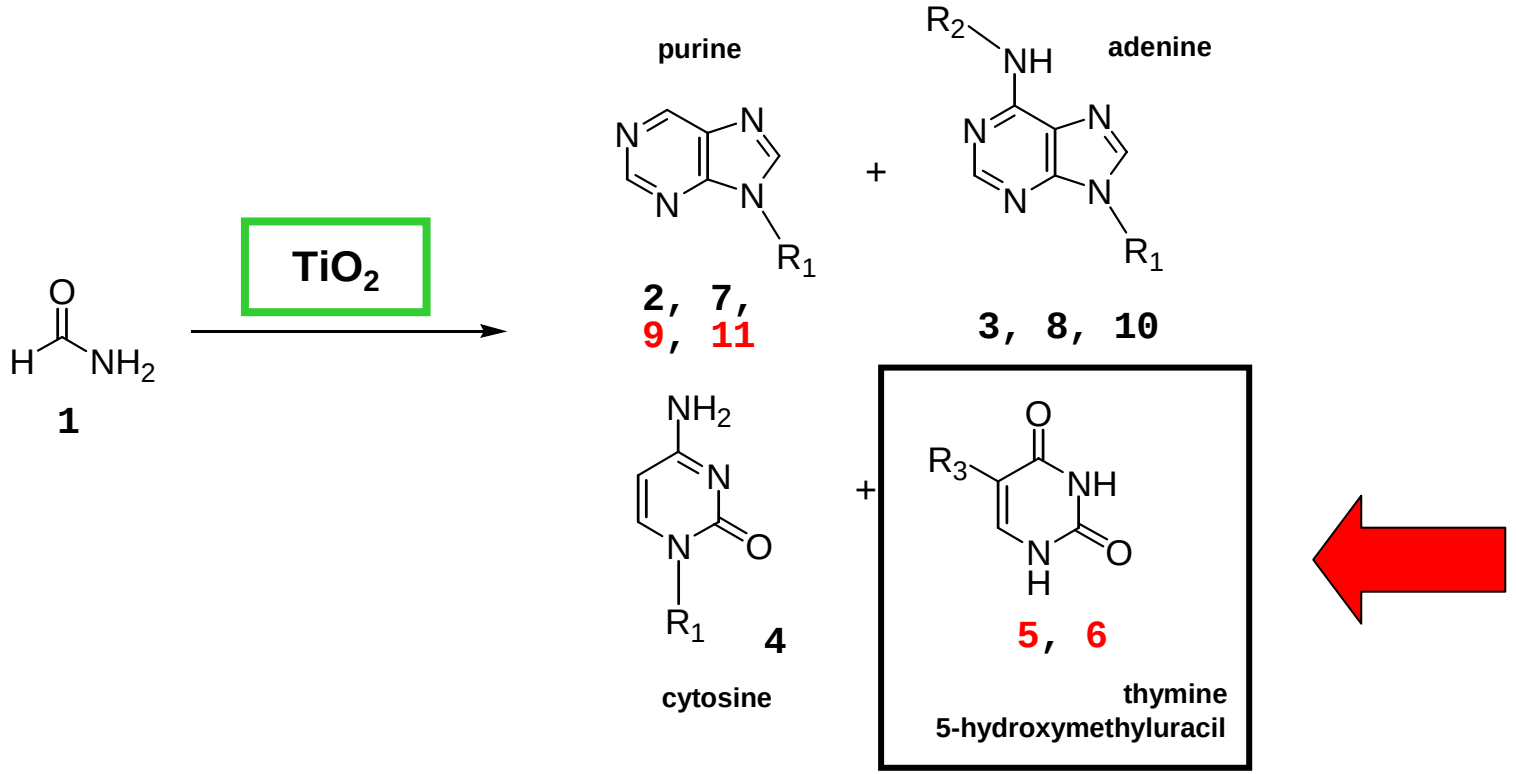
Uracil **8**



Formylpurine **9**

Montmorillonite: KP-10, K-30, KSF and Al-PILC

Synthesis of purine and pyrimidine bases, N^9-formylpurines, and acyclonucleosides from formamide



2, 3, 4: R_1= R_2= H. **5**: R_1= H; R_3= CH_3. **6**: R_1= H; R_3= CH_2OH. **7,8**: R_1= R_2= CHO. **9**: R_1= $COCH_2OH$. **10**: R_1= $COCH_2OH$; R_2= COH. **11**: R_1= $COCH(OH)CH_2OH$.

9 N^9-formylpurines

11 acyclonucleosides

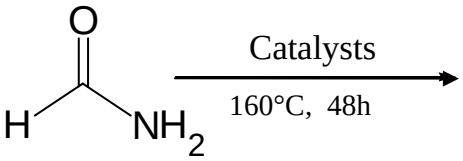
Silica
Alumina
Zeolite

Kaolin
$CaCO_3$

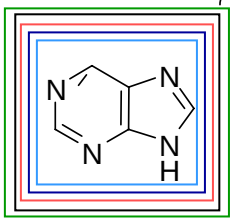
TiO_2

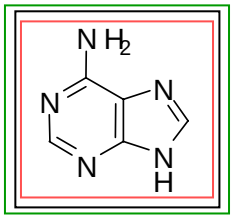
Montmorillonites

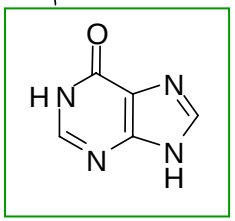
Cosmic Dust
Analogues



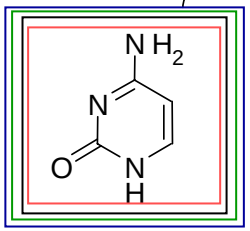
Purines

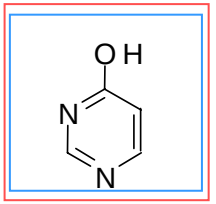

Purine

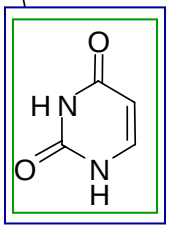

Adenine

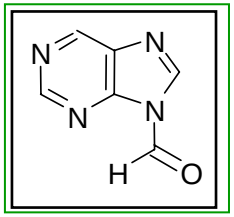

Hypoxanthine

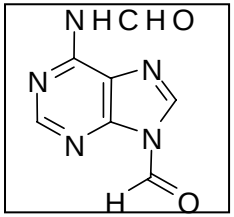
Pyrimidines

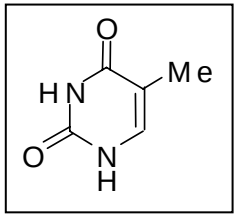

Cytosine

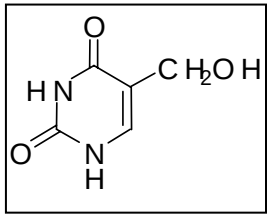

Hydroxypyrimidine

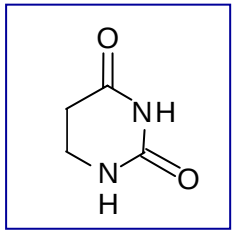

Uracil

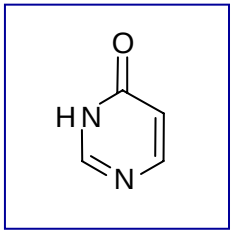

N9-Formylpurine


N,N-Diformyladenine

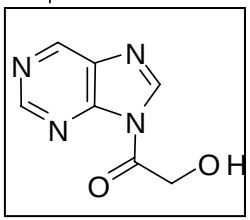

Thymine

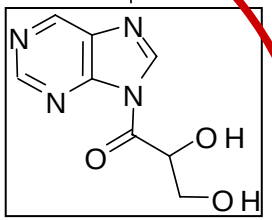

Hydroxymethyluracil

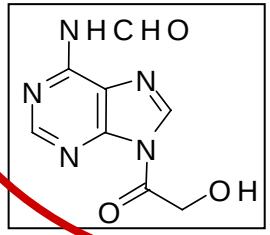

5,6-Dihydrouracil

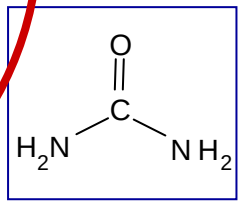

4-(3H)-pyrimidinone

Acyclonucleosides

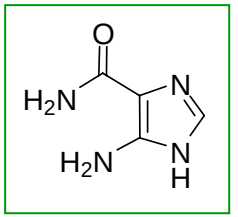


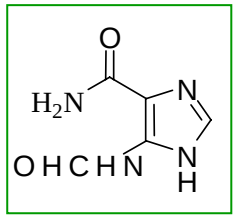





urea

Imidazoles


AICA

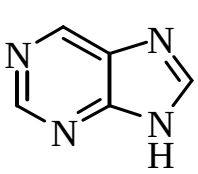

fAICA

phosphate minerals

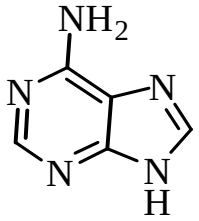
- Variscite $Al(PO_4)(H_2O)_2$
- Augelite $Al_2\ PO_4(H_2O)_3$
- Wavellite $Al_3(OH)_3(PO_4)_2(H_2O)_5$
- Hydroxylapatite $Ca_5(PO_4)_3OH$
- Hureaulite $Mn^{2+}{}_5(PO_3(OH)_2(PO_4)(H_2O)_4$
- Reddingite $Mn^{2+}{}_3(PO_4)_2(H_2O)_3$
- Purpurite $Mn^{3+}(PO_4)$
- Ludlamite $Fe^{2+}{}_3\ (PO_4)_2(H_2O)_4$
- Vivianite $Fe^{2+}{}_3(PO_4)_2(H_2O)_8$
- Strengite $Fe^{3+}(PO_4)(H_2O)_2$
- Cacoxenite $Fe^{3+}{}_{25}(PO_4)_{17}O_6(OH)_{12}(H_2O)_{75}$
- Libethenite $Cu^{2+}{}_2(PO_4)(OH)$
- Cornetite $Cu^{2+}{}_3(PO_4)(OH)_3$
- Tarbuttite $Zn_2(PO_4)(OH)$
- Monazite $Ce(PO4)$
- Montebrasite $Li[Al(PO_4)(OH)]$
- Beryllonite $Na[BePO_4]$
- Brasilianite $NaAl_3(PO_4)_2(OH)_4$
- Wardite $NaAl_3(OH)_4(PO_4)_2(H_2O)_2$
- Hydroxylapatite $Ca_5(PO_4)_3OH$

- Lazulite $Mg[Al(PO_4)(OH)]_2$
- Childrenite $Mn^{2+}[Al(PO_4)(OH)_2(H_2O)]$
- Triphylite $LiFe^{2+}(PO_4)$
- Eosphorite $Fe^{2+}[Al(PO_4)(OH)_2(H_2O)]$
- Vauxite $Fe^{2+}Al_2(PO_4)(OH)_2(H_2O)_6$
- Fairfieldite $Ca_2\ [Mn^{2+}(PO_4)(H_2O)\ _2]$
- Laueite $Mn^{2+}[Fe^{3+}{}_2(PO_4)_2(OH)_2(H_2O)_2](H_2O)_4(H_2O)_2$
- Rockbridgeite $Fe^{2+}Fe^{3+}{}_4(PO_4)_3(OH)_5$
- Fluorapatite $Ca_5(PO_4)_3F$
- Crandallite $CaAl_3(PO_4)_2(OH)_5{+}H_2O$
- Anapaite $Ca_2[Fe^{2+}(PO_4)_2(H_2O)_4]$
- Scholzite $CaZn_2(PO_4)_2(H_2O)_2$
- Turquoise $Cu^{2+}Al_6(PO_4)_4(OH)_8(H_2O)_4$
- Pyromorphite $Pb_5(PO_4)_3Cl$
- Autunite $Ca[(UO_2)\ (PO_4)]_2(H_2O)_{10\text{-}12}$
- Torbenite $Cu^{2+}[(UO_2\ (PO_4)]_2\ (H_2O)_8$
- Herderite $Ca[BePO_4F]$
- Pseudomalachite $Cu^{2+}{}_5\ (PO_4)_2(OH)_4$
- Calcioferrite $Ca_4MgFe_4(PO_4)_6(OH)_4(H_2O)_{13}$

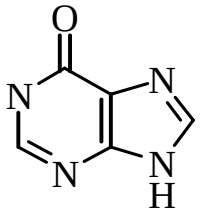
Synthesis of purine and pyrimidine bases from phosphate minerals



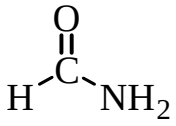
1 Purine

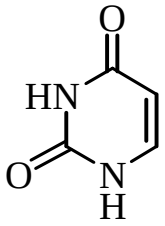


2 Adenine

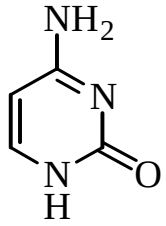


3 Hypoxanthine

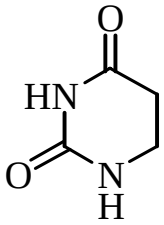




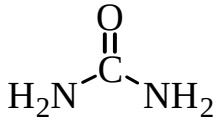
4 Uracil



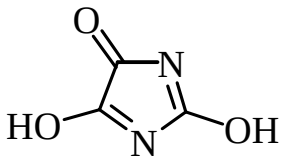
5 Cytosine



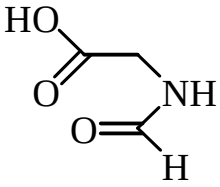
6 Dihydrouracil



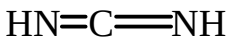
7 Urea



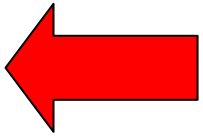
8 Parabanic acid



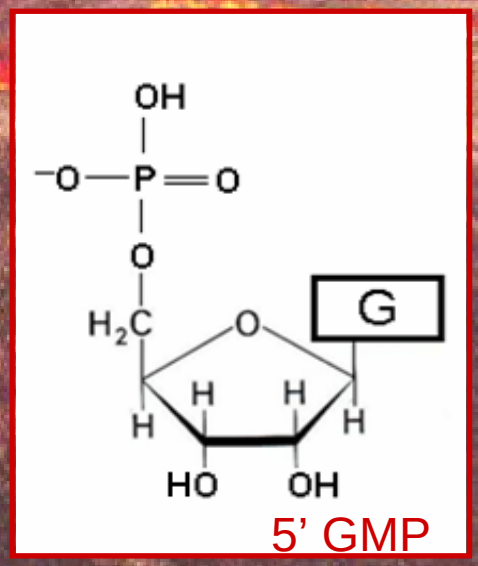
9 N-formylglycine



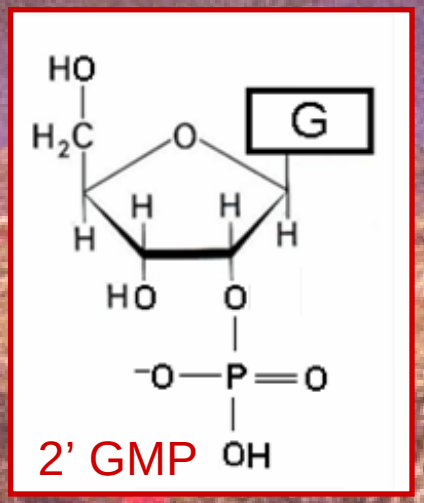
10 Carbodiimide

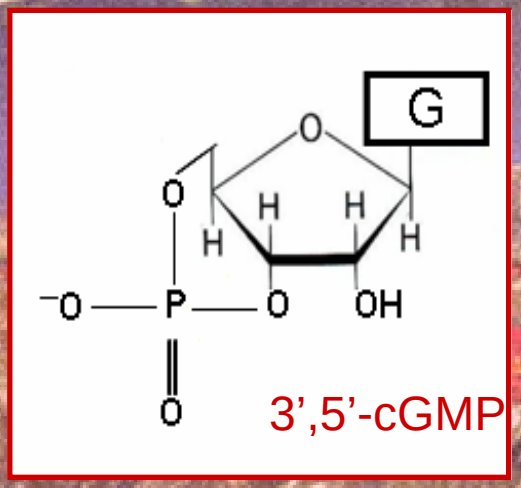


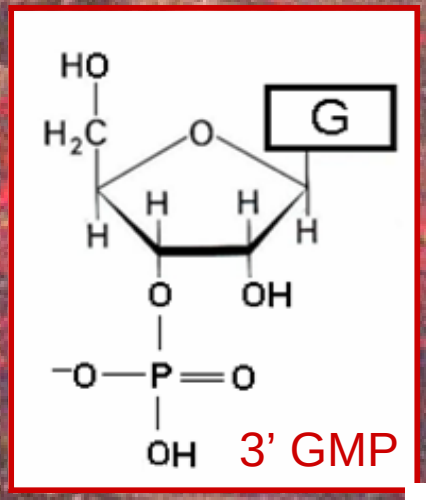
Spontaneous phosphorylation of nucleosides

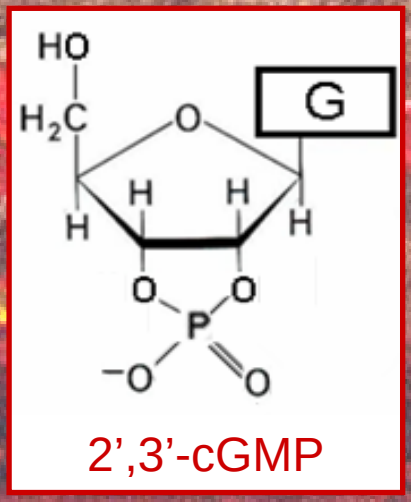


5’ GMP







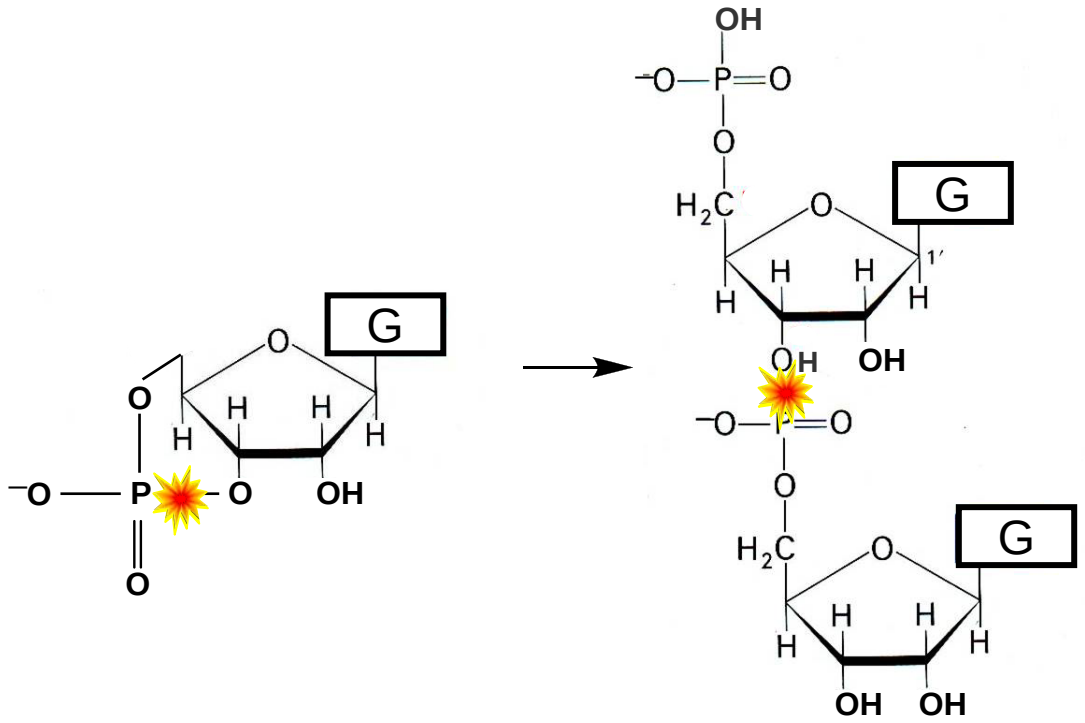


Costanzo *et al*. J. Biol. Chem. 2007

RNA polymerization in water

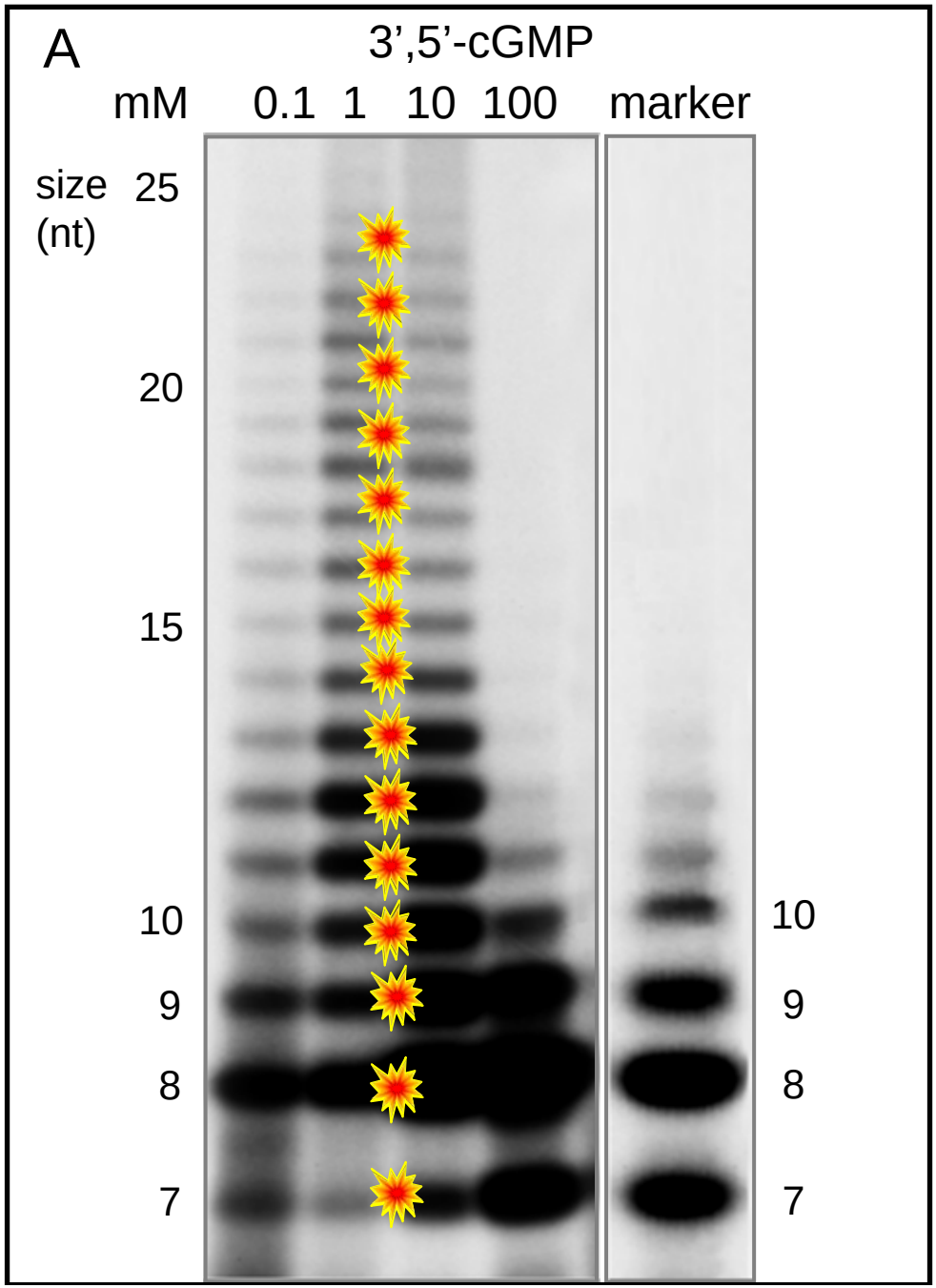
Costanzo et al. J. Biol. Chem. 2009

Polymerizing 3',5'-cyclic GMP



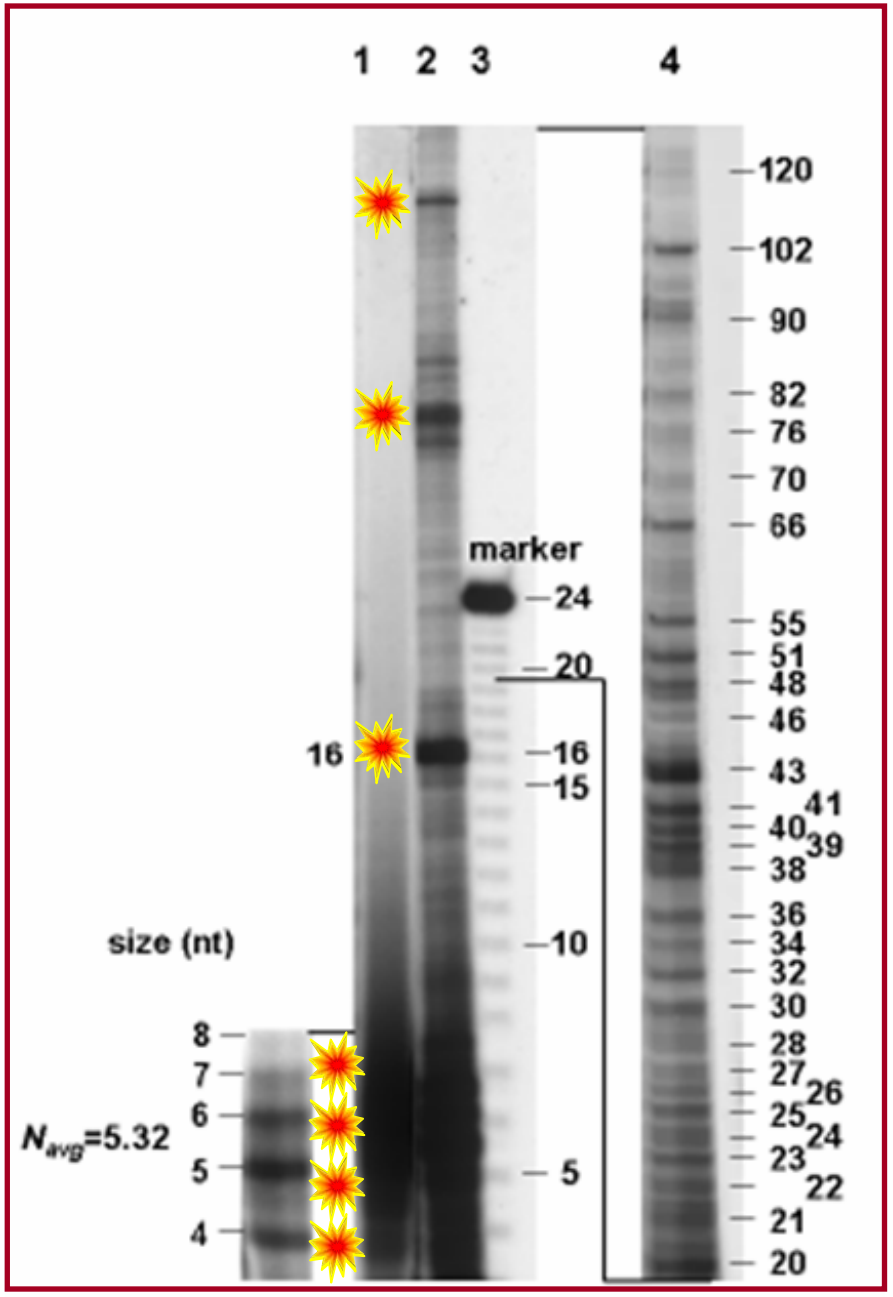
Non-enzymatic polymerization of 3’,5’-cGMP

1hr ; 85°C;
TrisHCl pH 8,2

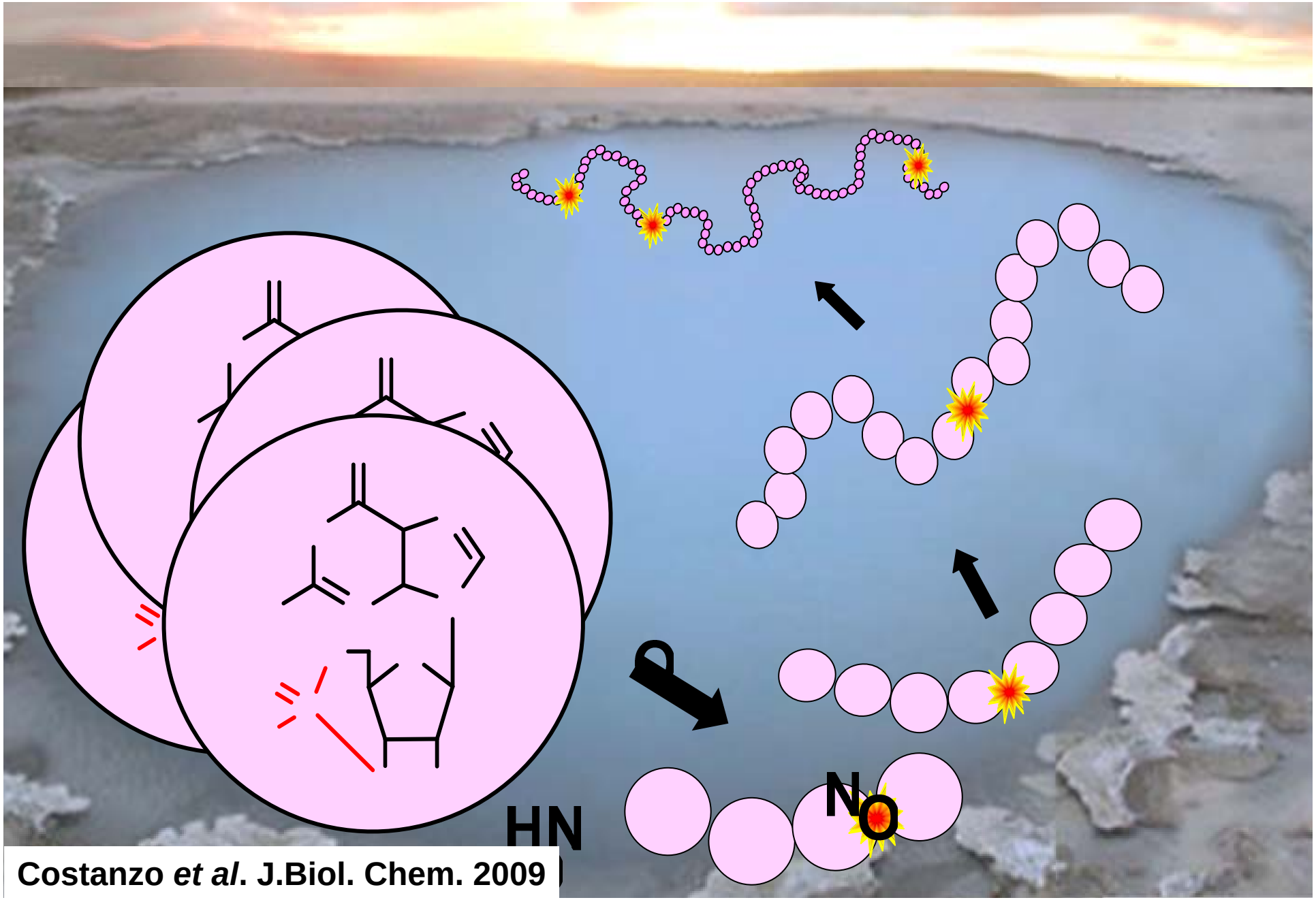


Non-enzymatic polymerization of 3’,5’-cAMP

85°C; TrisHCl pH 8,2



the warm little pond



Costanzo *et al*. J.Biol. Chem. 2009

Non-enzymatic mechanisms for the generation of long RNA sequences in water

- **Synthesis of RNA chains from cyclic nucleotides**
- **RNA chain extension**
- **RNA ligation**

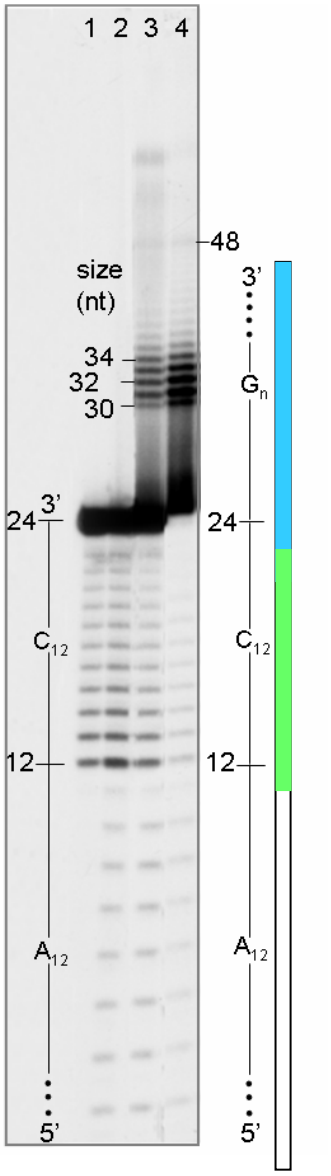
- **RNA stability in different conditions of temperature and pH**

RNA chain extension in water

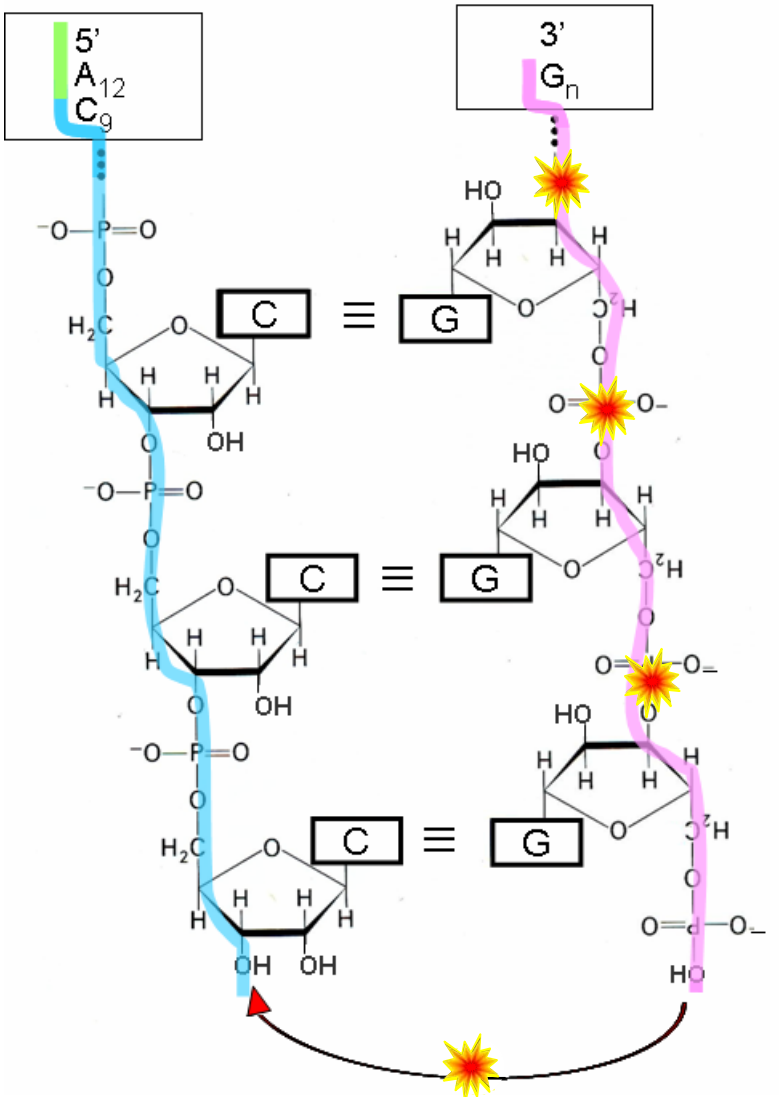
Costanzo *et al*. J.Biol. Chem. 2009

Synthesis of oligo Gs from 3′,5′-cGMP in the presence of 5′$A_{12}C_{12}$3′

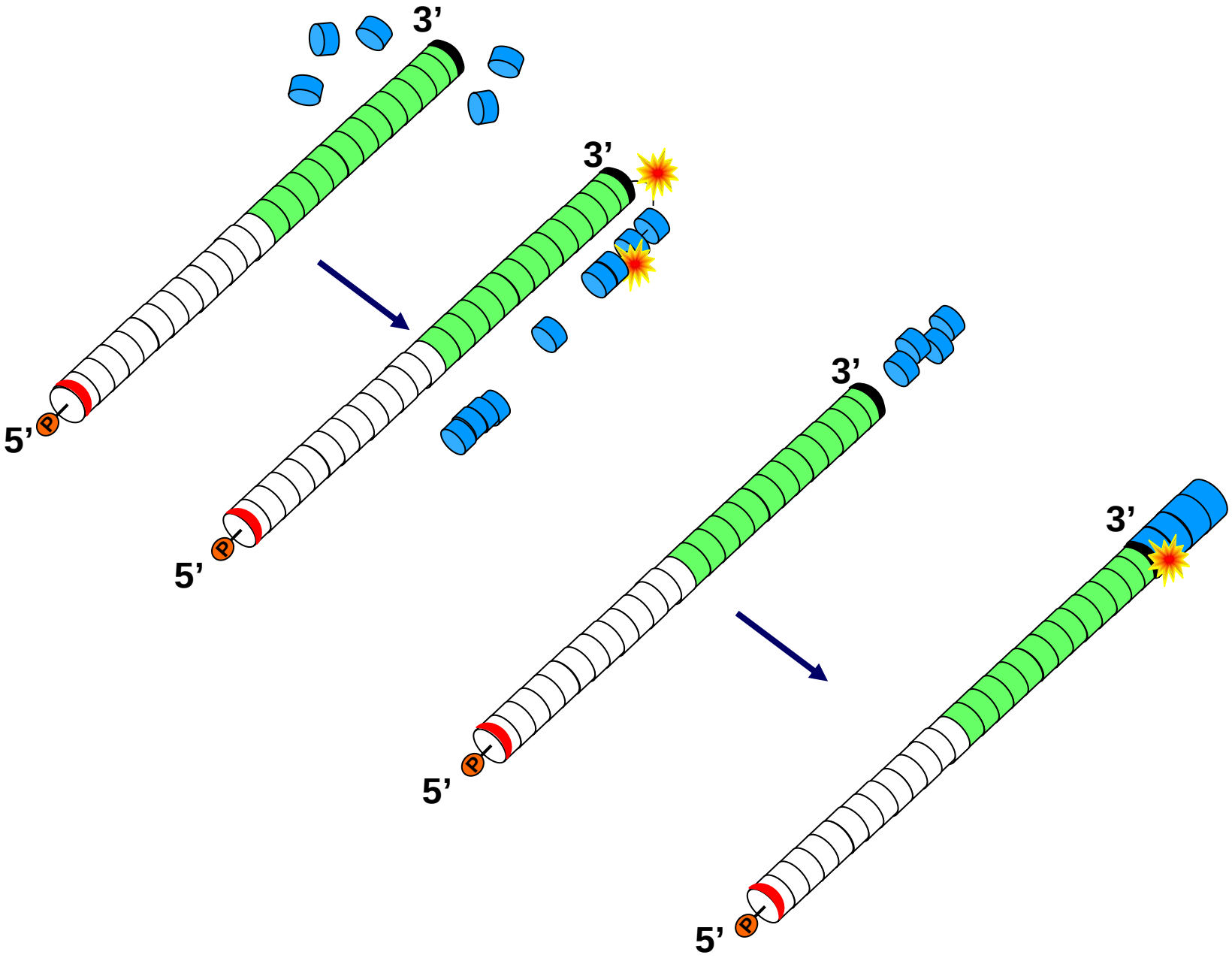
Navg=32,75



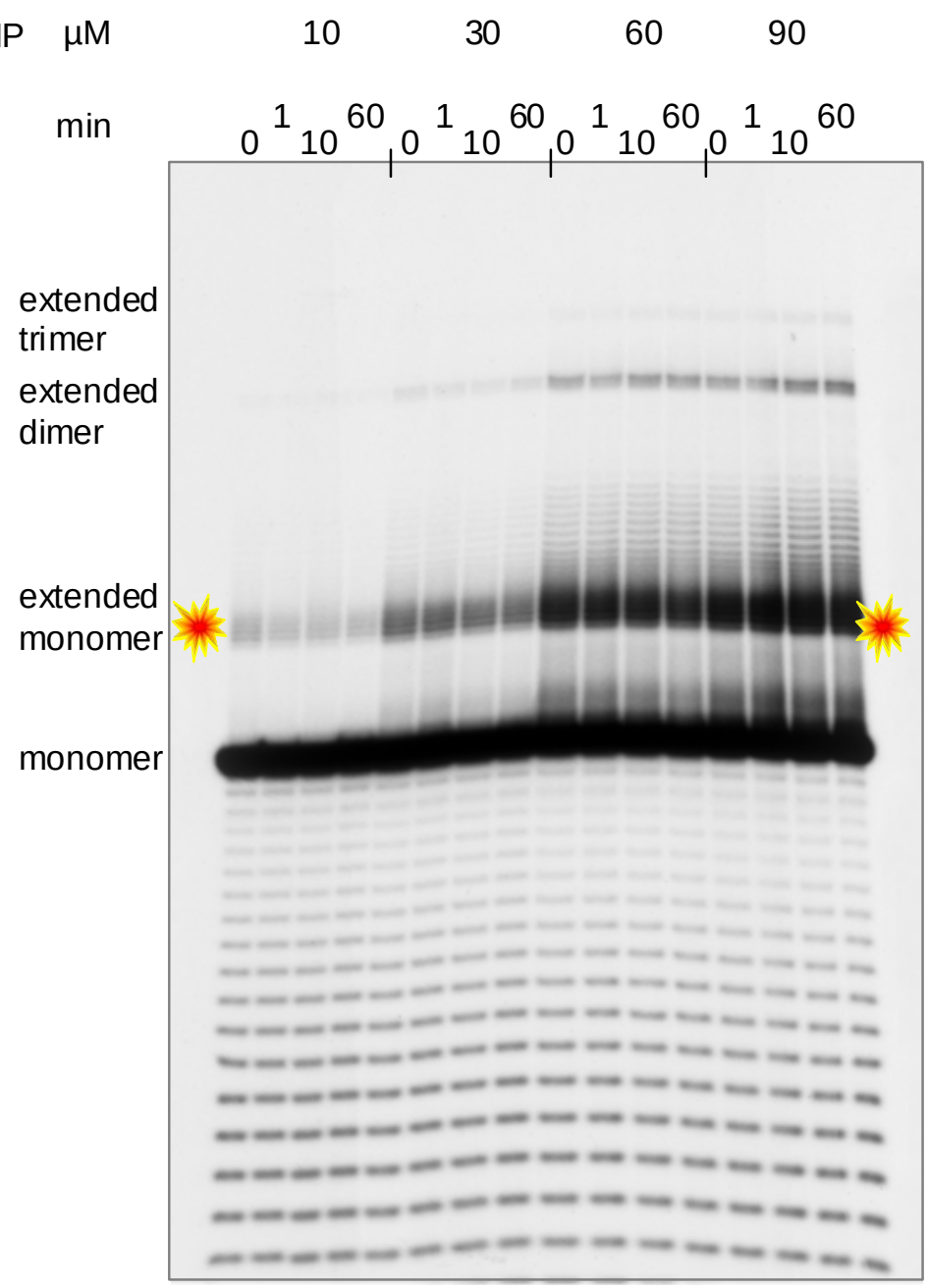
Polymerizing 3′,5′-cyclic GMP on a 5′$A_{12}C_{12}$3′ oligo



The plausible mechanism for sequence extension

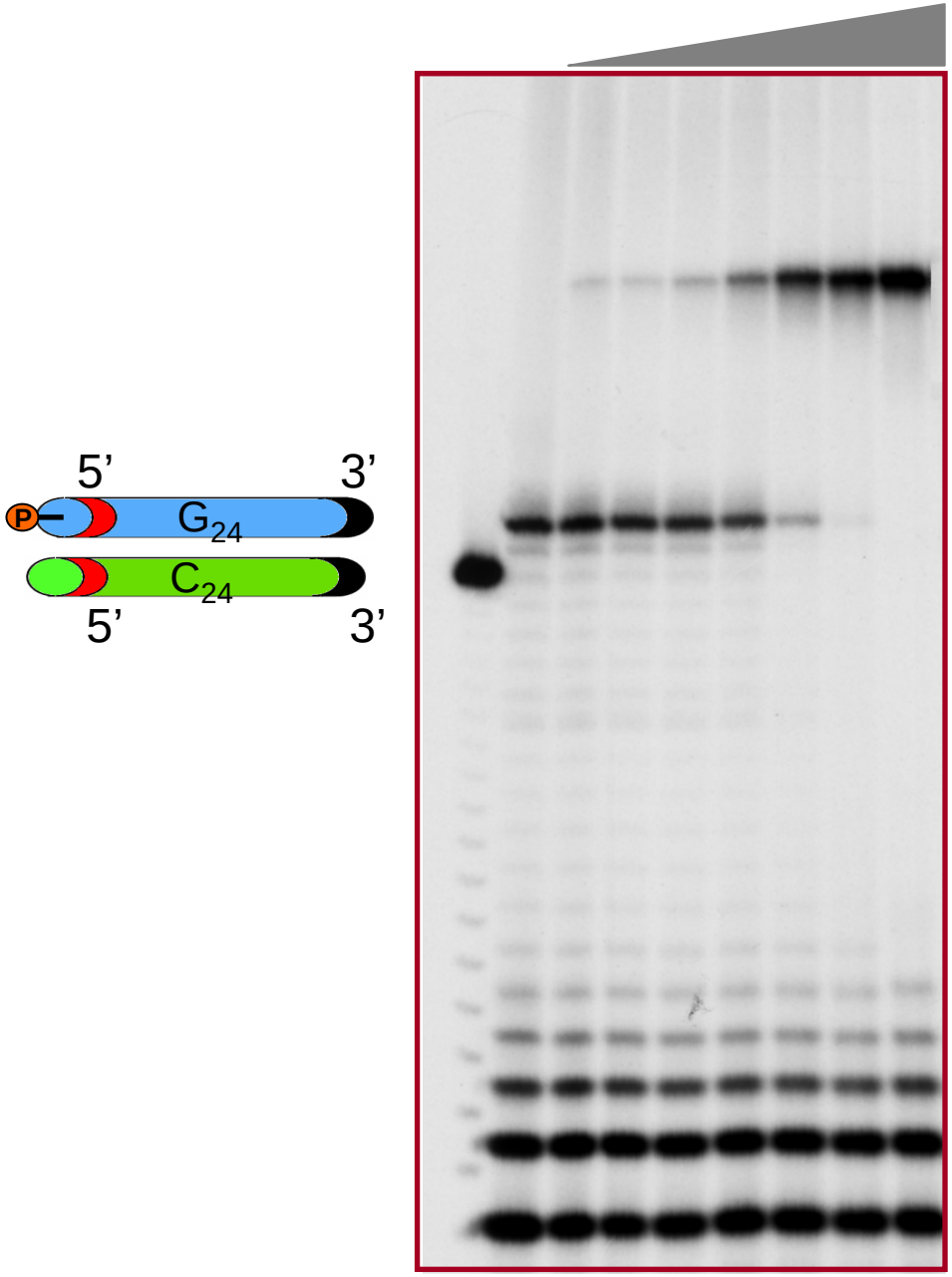


An explosive, concentration-dependent chain-extension reaction

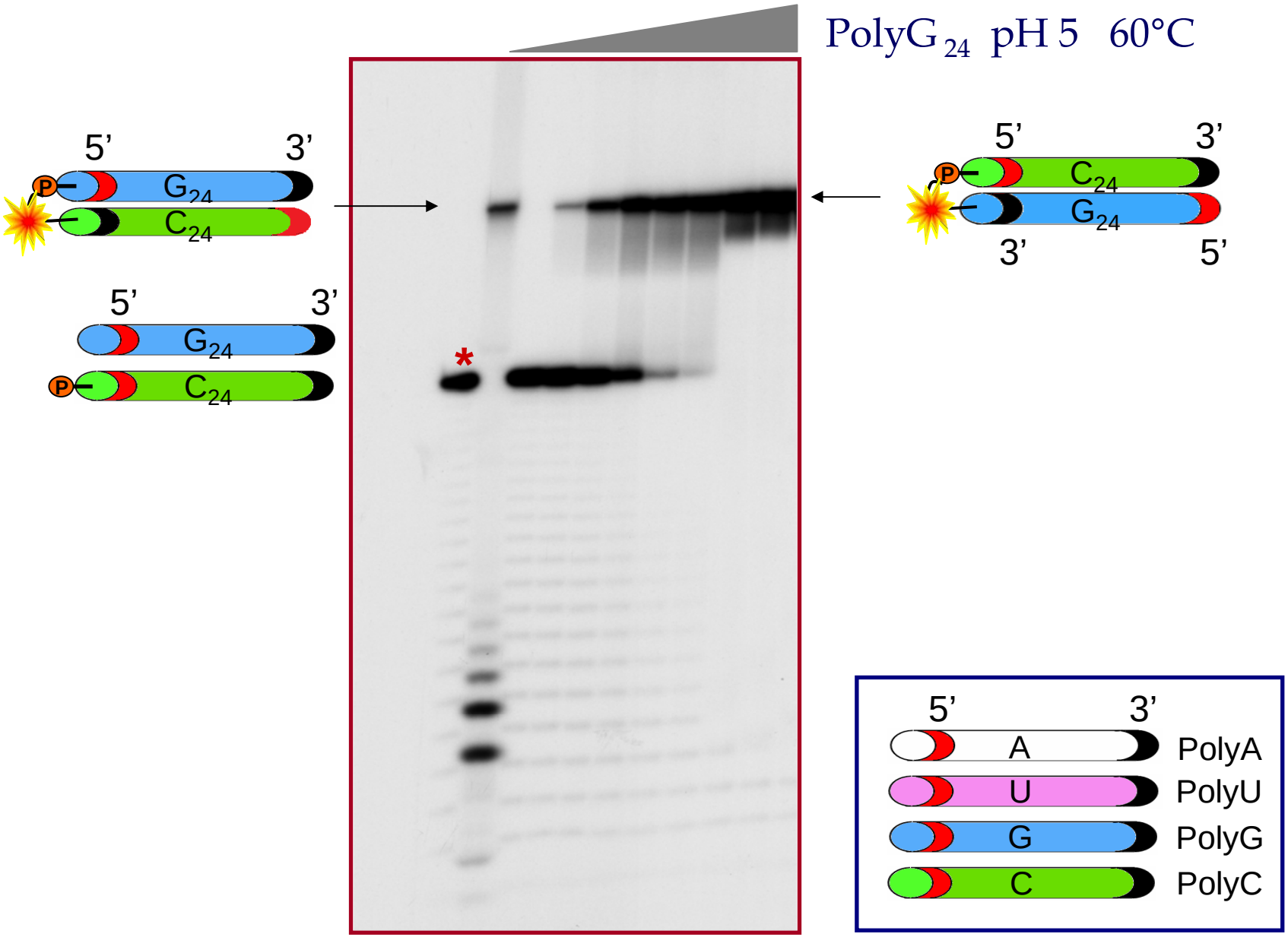


Sequence-directed terminal ligation

PolyG(P) + PolyC sequence-directed terminal ligation



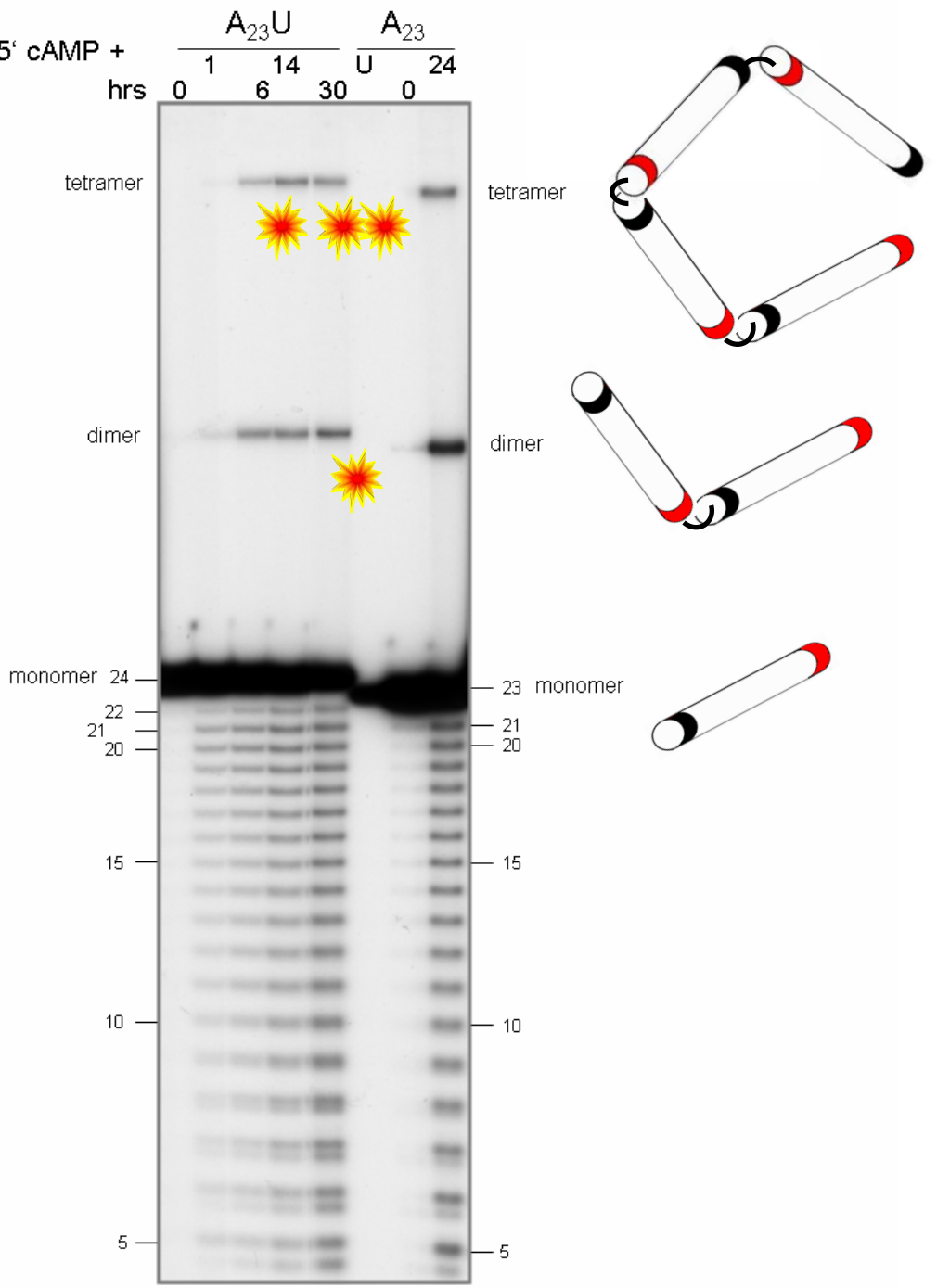
PolyC(P) + PolyG sequence-directed terminal ligation



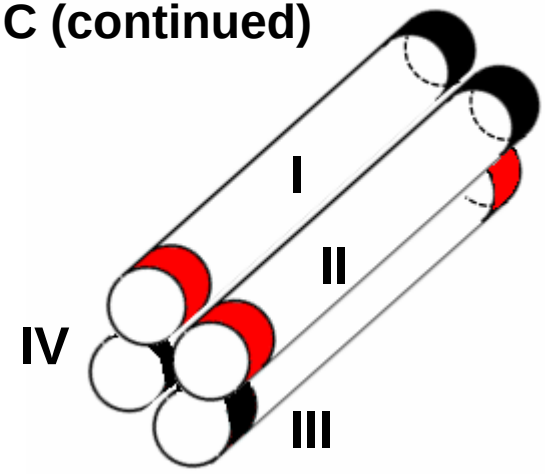
Stacking-directed terminal ligation

Pino et al. J. Biol. Chem. 2008

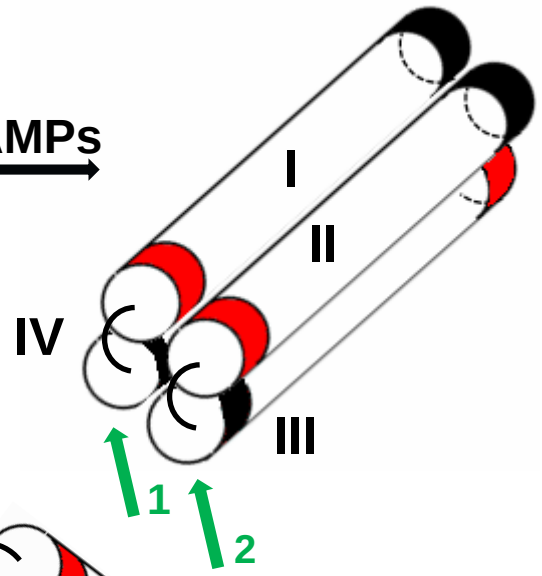
RNA ligation in H_2O 23-, 24-mer



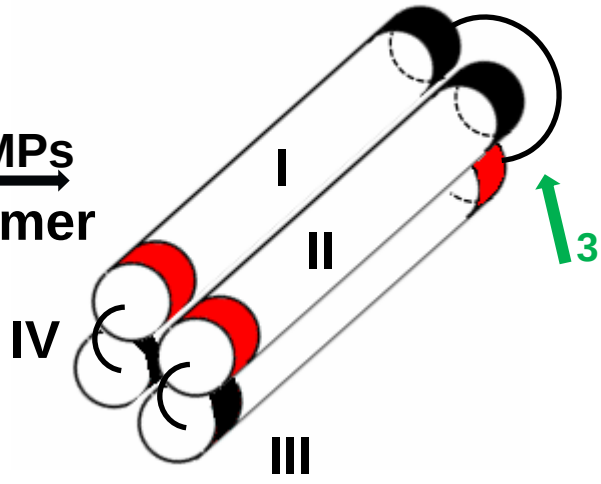
C (continued)



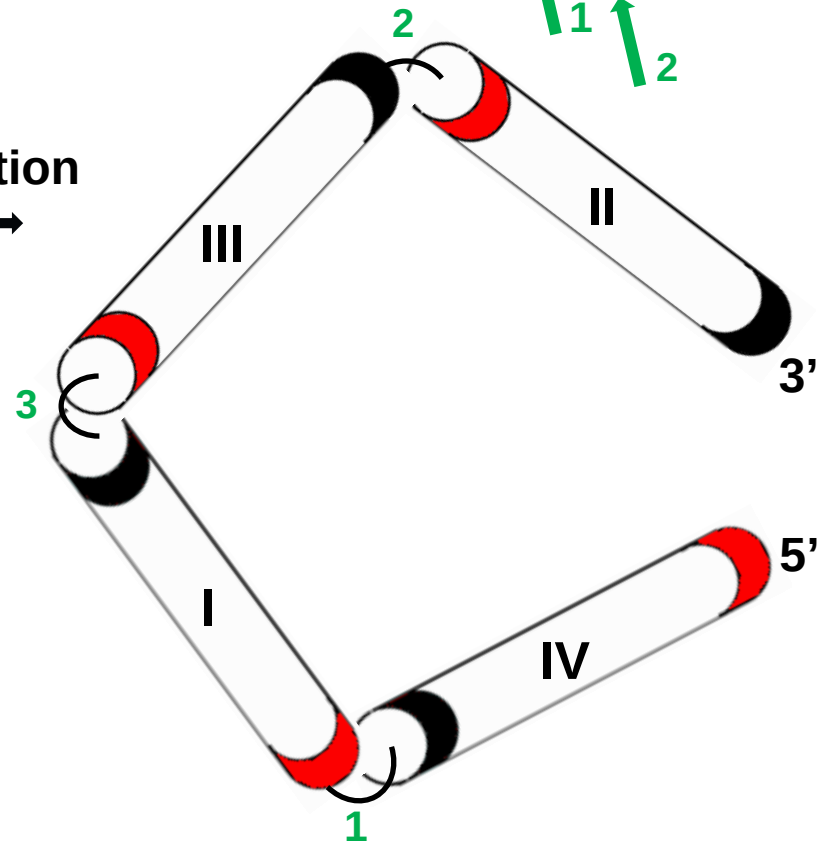
AMPs

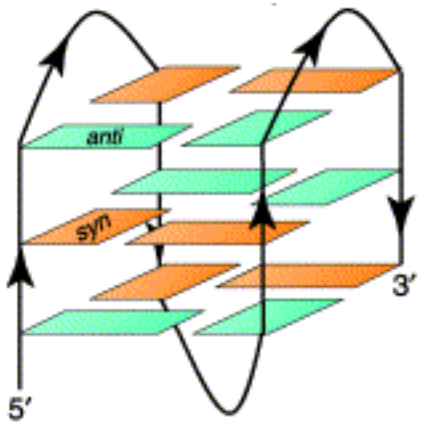


AMPs
>10mer



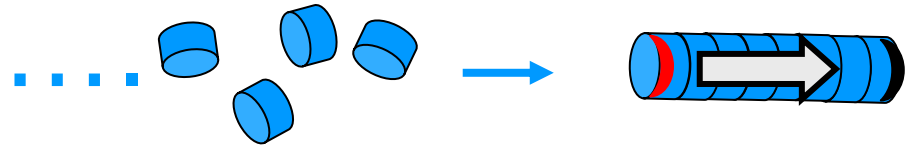
resolution



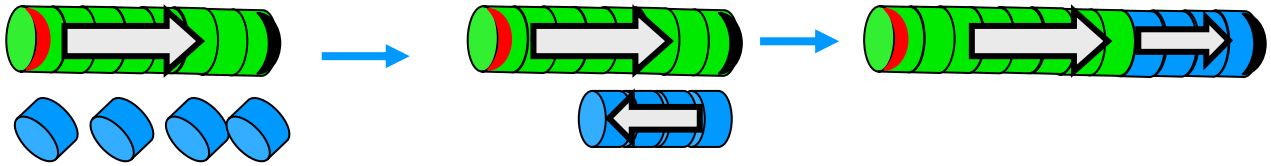


Non-enzymatic mechanisms for the generation of long RNA sequences in water

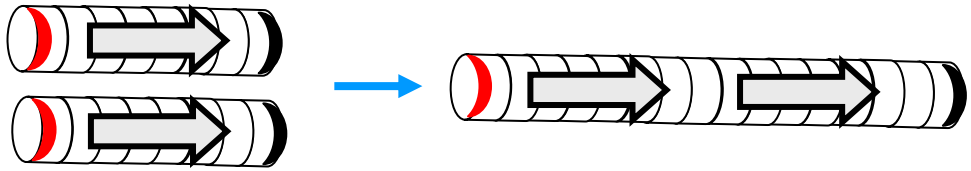
RNA synthesis

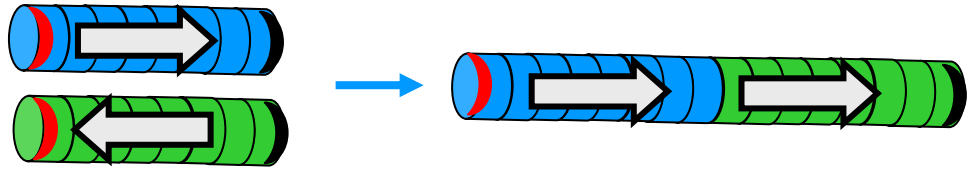


RNA chain extension



RNA ligation

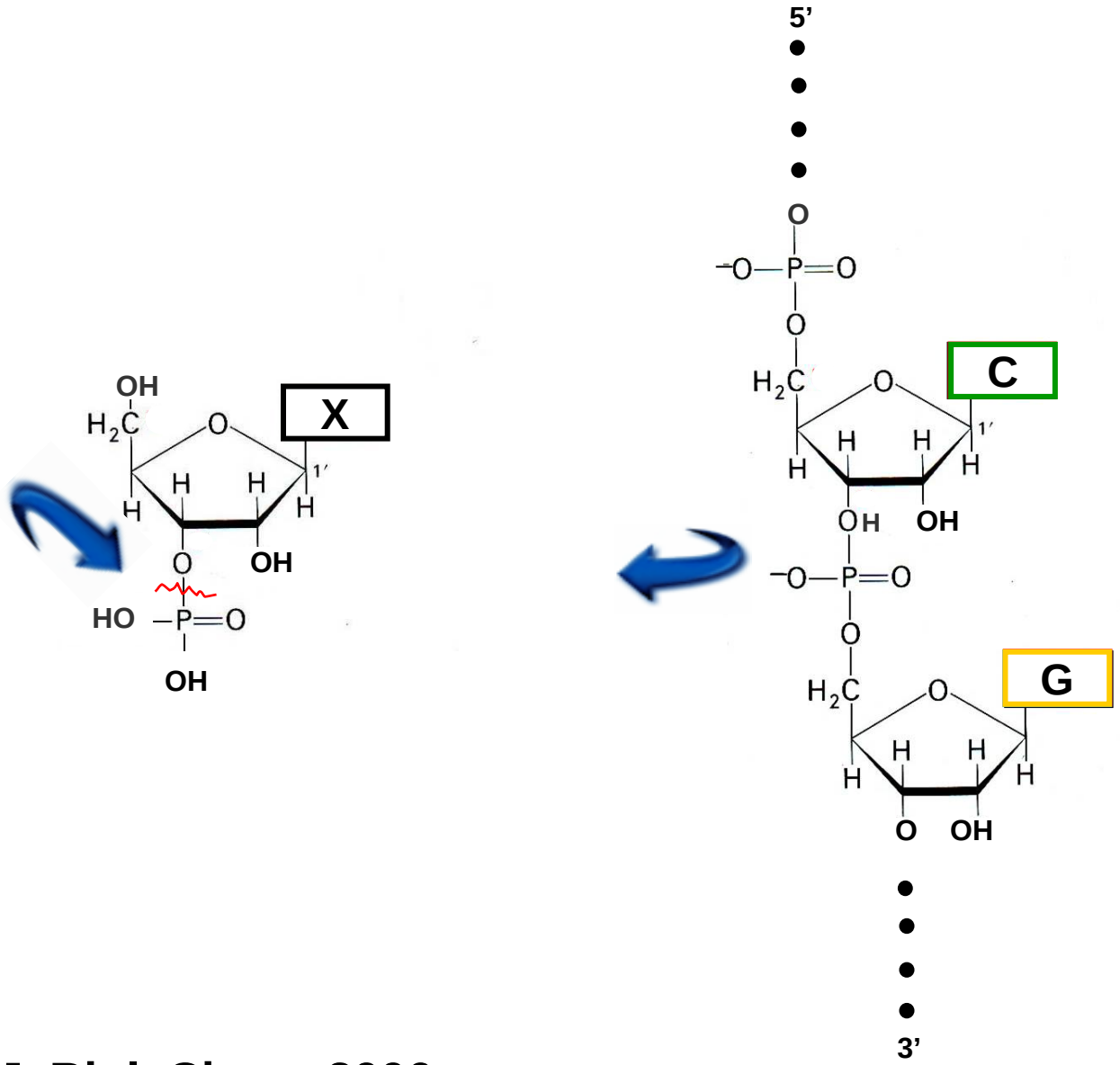




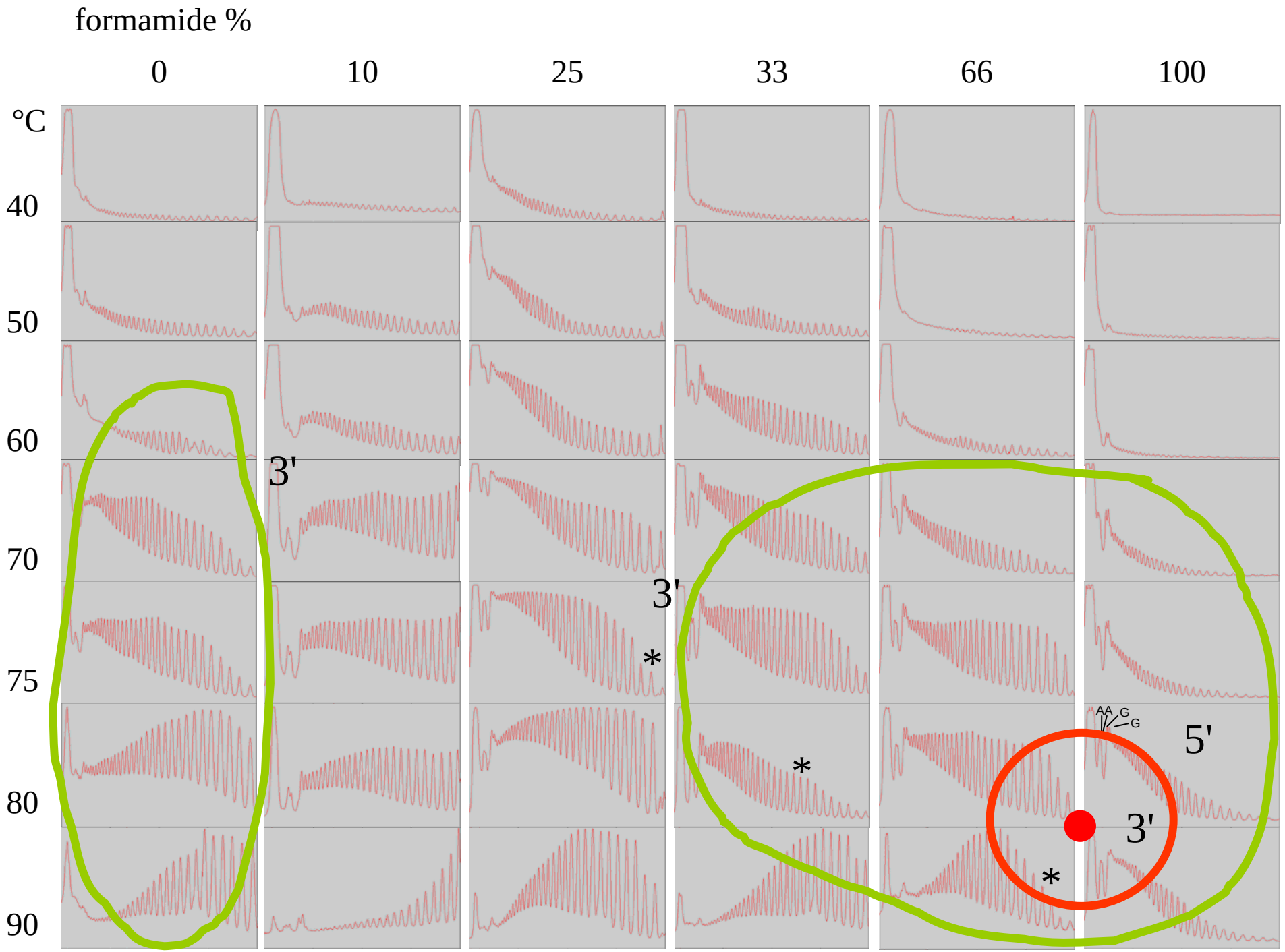
Combinations thereof → heterogeneous sequences

RNA multiplication in water

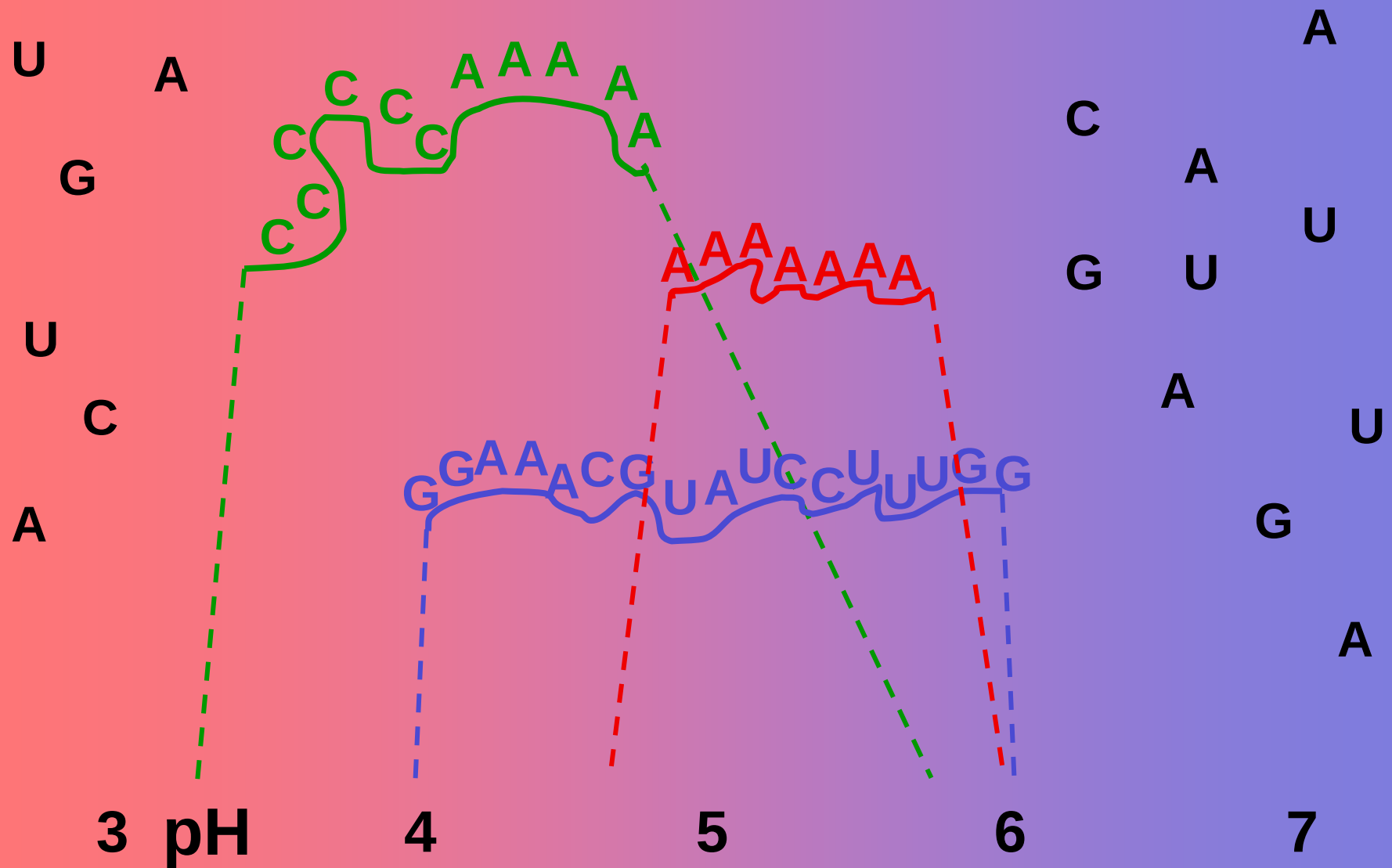
Differential stability of phosphoester bonds in ribo-monomers and oligomers



Saladino et al. J. Biol. Chem. 2006


formamide %
0
10
25
33
66
100
°C
40
50
60
70
75
80
90
3'
3'
*
*
*
AA
G
G
5'
3'

Environment induces selection for sequence complexity



Ciciriello *et al*. Biochemistry 2007

“Something came from nothing because it is more stable than nothing”

The Comprehensible Cosmos, Victor Stenger

Directed Assembly of One-Dimensional Nanostructures into Functional Networks

Yu Huang,[1]* Xiangfeng Duan,[1]* Qingqiao Wei,[1]
Charles M. Lieber[1,2]†

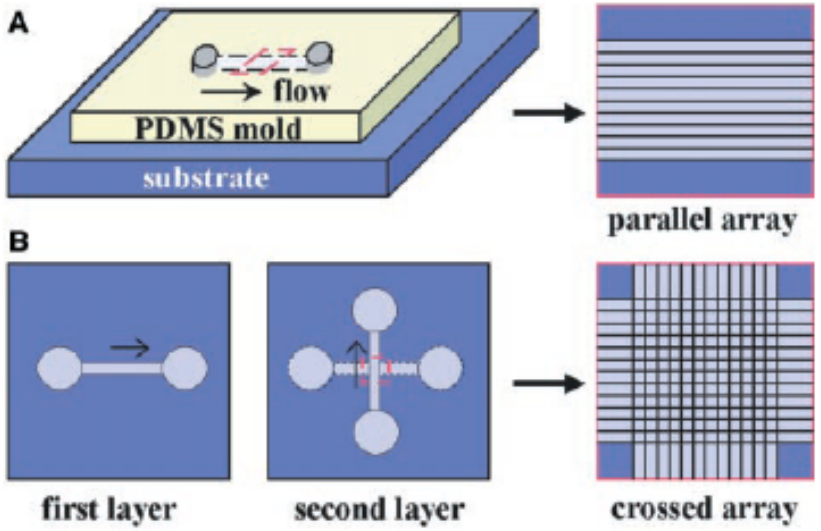
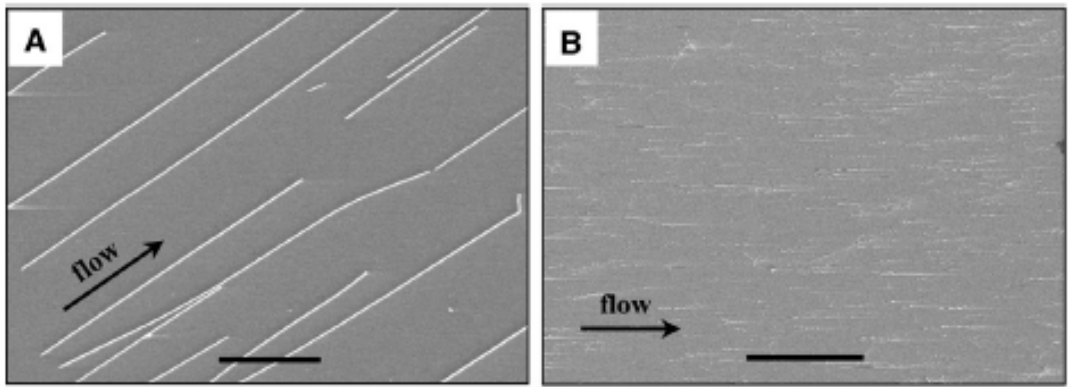
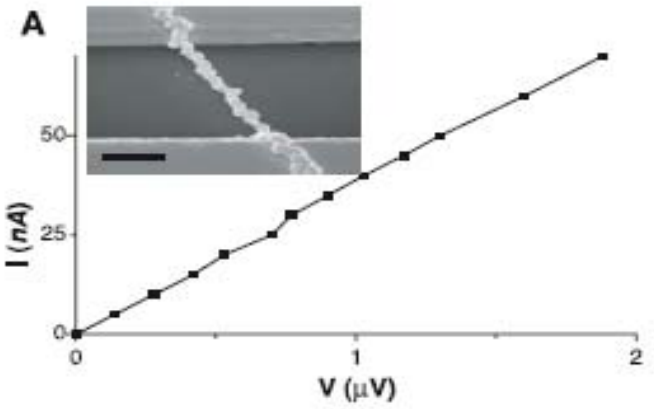


Fig. 1. Schematic of fluidic channel structures for flow assembly. (**A**) A channel formed when the PDMS mold was brought in contact with a flat substrate. NW assembly was carried out by flowing an NW suspension inside the channel with a controlled flow rate for a set duration. Parallel arrays of NWs are observed in the flow direction on the substrate when the PDMS mold is removed. (**B**) Multiple crossed NW arrays can be obtained by changing the flow direction sequentially in a layer-by-layer assembly process.





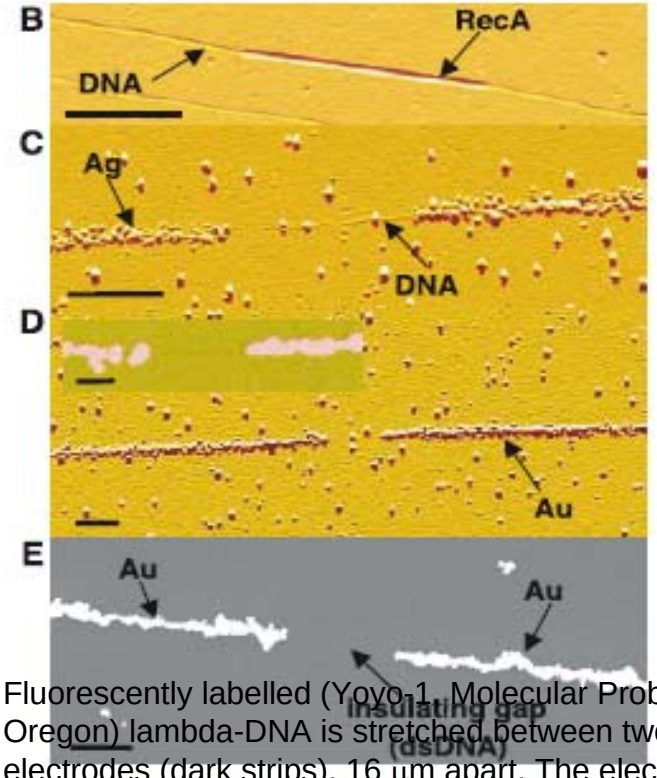
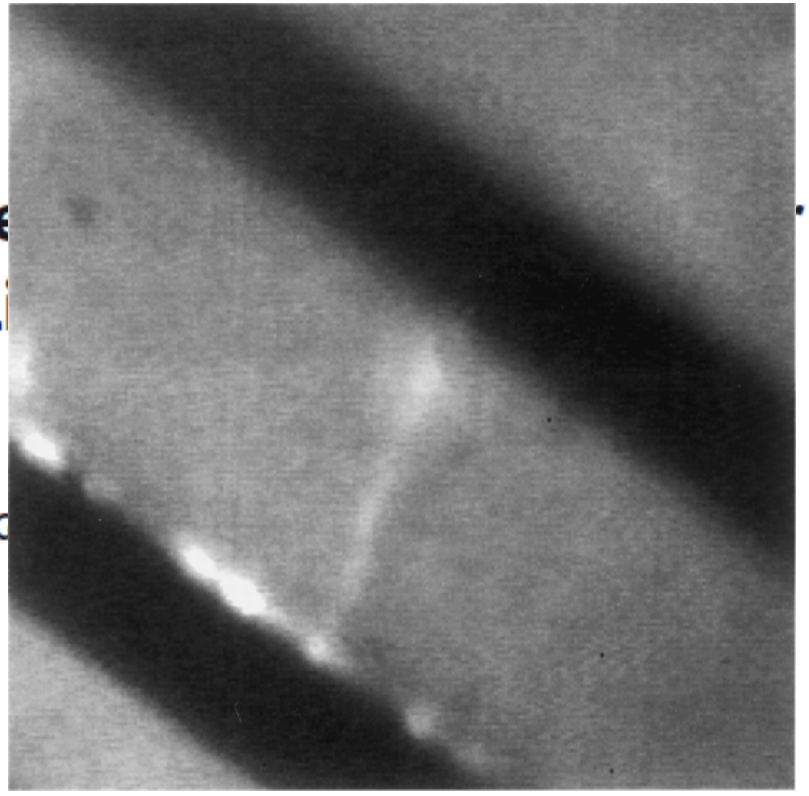


Fig. 2. Sequence-specific molecular lithography on a single DNA molecule. (A) Two-terminal current-voltage (*I-V*) curve of a DNA-templated gold wire.

Directed Assembly of One-Dimensional Nanostructures into Functional Networks

Yu Huang,[1]* Xiangfeng Duan,[1]* Qingqiao Wei,[1]
Charles M. Lieber[1,2]†

26 JANUARY 2001 VOL 291 SCIENCE



Fluorescently labelled (Yoyo-1, Molecular Probes, Eugene, Oregon) lambda-DNA is stretched between two gold electrodes (dark strips), 16 μm apart. The electrodes are connected to large bonding pads 0.25 mm away.

US005561071A

United States Patent [19]

Hollenberg et al.

[11] **Patent Number: 5,561,071**

[45] **Date of Patent: Oct. 1, 1996**

[54] **DNA AND DNA TECHNOLOGY FOR THE CONSTRUCTION OF NETWORKS TO BE USED IN CHIP CONSTRUCTION AND CHIP PRODUCTION (DNA-CHIPS)**

[76] Inventors: **Cornelis P. Hollenberg**, Chopinstrasse 7, 4000, Düsseldorf, Germany; **Ernesto di Mauro**, Via Andrea Fulvio 10, 00162, Rome, Italy

[21] Appl. No.: **532,542**

[22] Filed: **Sep. 25, 1995**

Related U.S. Application Data

[63] Continuation of Ser. No. 116,556, Sep. 7, 1993, abandoned, which is a continuation of Ser. No. 22,615, Feb. 19, 1993, abandoned, which is a continuation of Ser. No. 552,938, Jul. 16, 1990, abandoned.

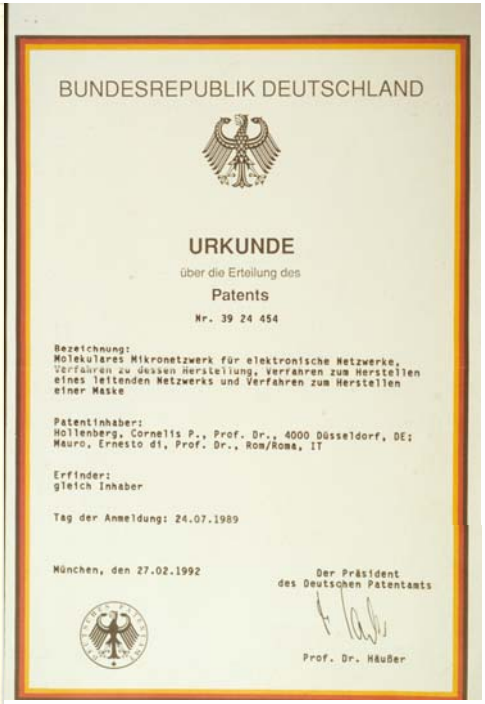
[30] **Foreign Application Priority Data**

Jul. 24, 1989 [DE] Germany 39 24 454.7

[51] **Int. Cl.**[6] **H01L 51/40**

[52] **U.S. Cl.** **437/1**; 435/810; 437/15; 437/16; 437/35; 437/36; 437/38; 437/51; 437/54; 437/80; 437/225; 437/238; 536/22.1; 536/25.3; 935/77; 935/88

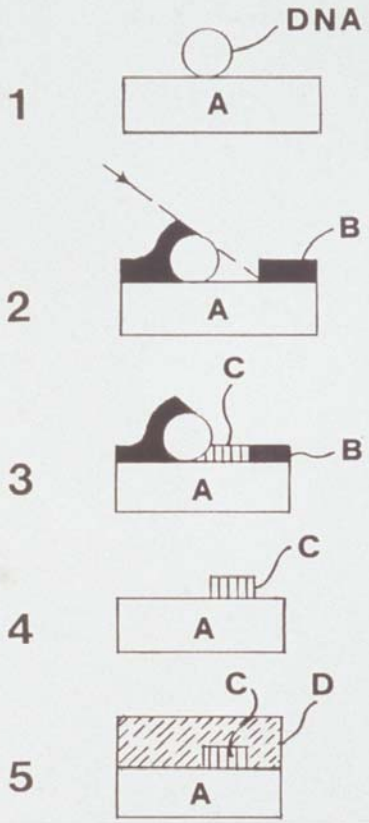
[58] **Field of Search** 435/6, 810, 287, 435/299; 536/22.1, 25.3; 437/1, 15, 16,



D. Eigler et al., "An Atomic Switch Realized With The Scanning Tunnelling Microscope," Nature, vol. 352, pp. 600–603 (1991).

A. Oliphant et al., "Defining the Sequence Specificity of DNA–Binding Proteins by Selecting Binding Sites from Random–Sequence Oligonucleotides: Analysis of Yeast GCN4 Protein," Molecular and Cellular Biology, 9:2944 (1989).

C. Cantor et al., "Orientation in Electric Fields," Biophysical Chemistry part II, 665–668 (1980).



子は、以下の方法によりマトリックス（この上に核酸回路網が形成される）に結合させることができる：

(1)　マイクロマニピュレーターを用いて特異的蛋白（即ちラムダー蛋白リプレッサー；下記を参照）溶液の微細な１滴を、ポリエチレンのような疎水性表面の上にのせ、乾燥させる。

(2)　配列６は自己アニーリングした二本鎖構造の左の末端に位置するような配列で、配列（４）

3' and 5' indicate the 2 extremities of the nucleic acid strand. The enzymatic polymerization of DNA by the enzyme DNA polymerase (ref.7) proceeds by addition of monomers to the 3'-extremity (see ref.1). The letters G,A,C,T are acronyms that indicate the monomeric constituents of the DNA strand; they are nucleotide monophosphates containing respectively a purine (guanine for G, adenine for A) or a pyrimidine (cytosine for C,, thymine for T) residue. In DNA polymers these compounds can base pair specifically: G couples always with C, A with T. Therefore a self-annealing reaction in a solution containing the appropriate buffer (2x SSC solution, ref.8 p.447) at 20° C. will produce the molecule.

(2)

The left extremity of molecule (2) is the DWIP, the right extremity is the growing point (that is the point onto which additional hybridization or synthetic reactions can be performed in order to elongate the chain and/or create branch points or switches. Elongation may be obtained by hybridization of a preformed DNA molecule or a reaction of DNA synthesis. Hybridization of nucleic acids is a procedure that exploits the tendency of nucleic acids to anneal to double strand structures (according to the rules mentioned above: A with T, G with C), if the complementary order of the nucleotides that compose the DNA sequence permits it.

One synthesizes according to the procedure mentioned above the following molecule:

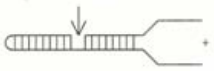
GATAAAACCTTCCATAACAAAGTGGTTGAA (3)

The hybridization reaction between molecules (2)+(3) will produce molecule (4):

(4)

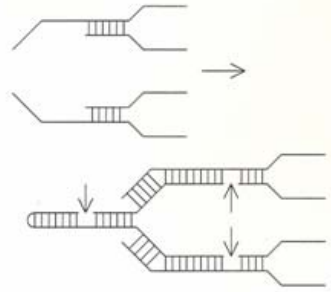
This molecule produced by synthesis and hybridization has one DWIP (left) (defined above as "blunt end") and a branched extremity (right). This branched extremity now provides two different growing points that can be used for further elongation and branching of the molecule, to produce a network (Scheme 1)). Many DNA sequences can lead to the shown below structure. The length is variable.

Scheme 1:



-continued

Scheme 1:



Single strand interruptions in the DNA strands (indicated in Scheme 1 by the arrows), can be easily filled up by the reaction of the enzyme DNA ligase (commercially available, i.e., from Bethesda Research Laboratories, Boehringer Mannheim, etc, see refs. 8,9). The synthesis of oligonucleotides (molecules 1 and 3) can be performed with commercially available apparatus (i.e., from Applied Biosystems or New Brunswick Scientific Company).

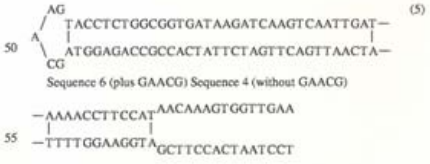
The DWIP can be fixed to a solid matrix by several techniques e.g., locally fixed charged molecules or sequence specific DNA binding proteins (as bacteriophage DNA binding proteins, Adenovirus binding protein, lac repressor or synthetic DNA binding proteins) or covalent chemical binding.

Outline 2

A DNA molecule such as molecule (4) described in outline 1 can be fixed by the following procedure to a matrix onto which the nucleic acid network will be formed:

(i) Place, by the use of a micromanipulator, a microdrop of a solution of a specific protein (i.e. lambda-protein repressor; see below) on a hydrophobic surface like polyethylene and let it dry.

(ii) Synthesize a molecule (5) which contains the sequence (4) and (6) in such an arrangement that sequence 6 is located at the left end of the self-annealed double strand structure:

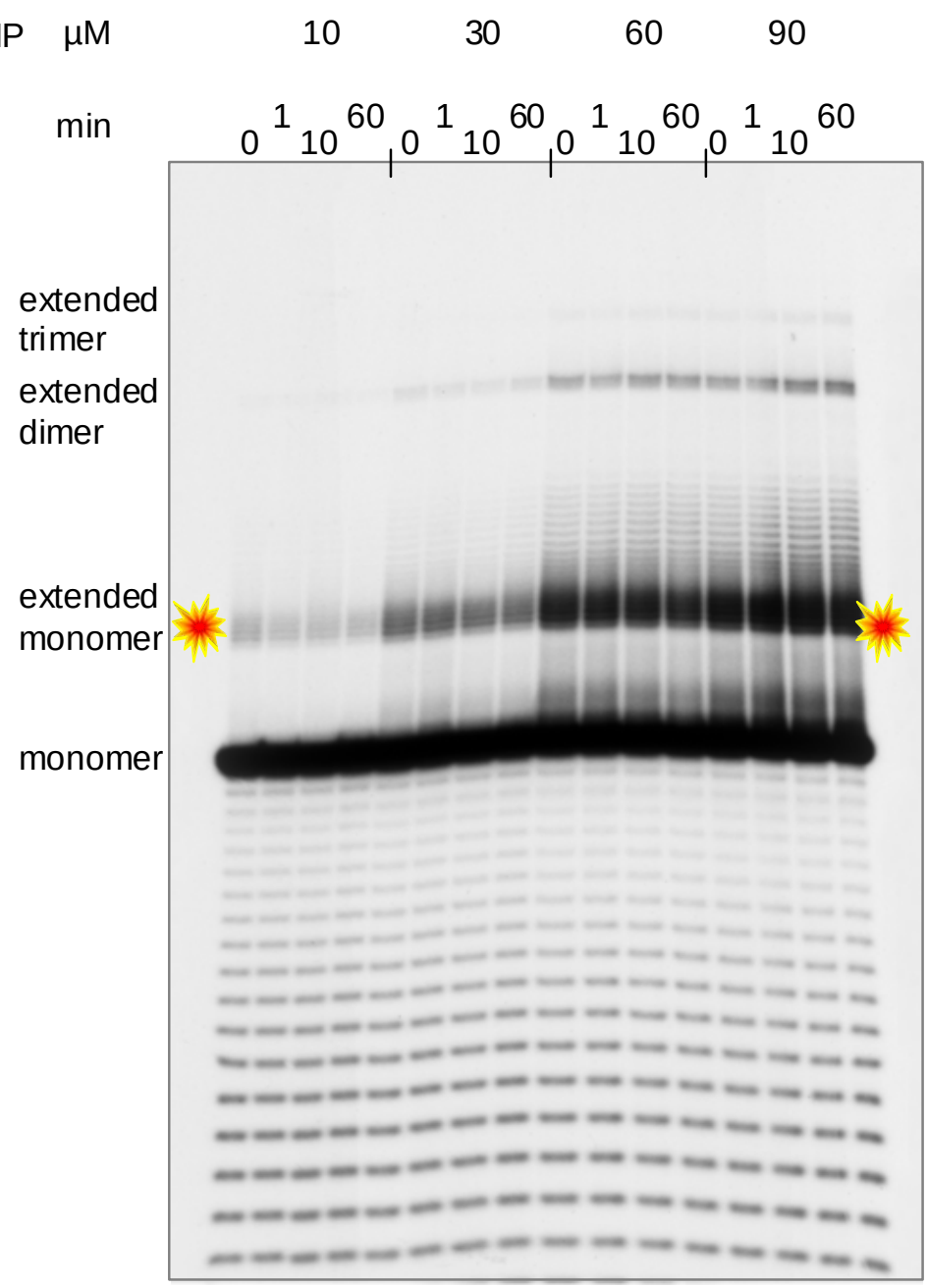


(5)

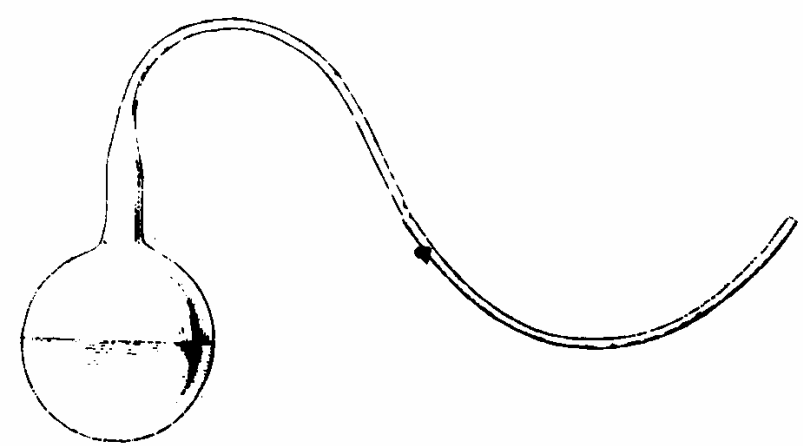
(iii) Treat the hydrophobic surface with a solution of DNA molecule (5). The specific binding of the DNA molecule to the protein molecule is ensured by the use of the specific DNA-protein interaction. Specificity of such interaction is a well-known phenomenon in biological processes and several DNA-protein interaction systems can be chosen, as detailed in the following paragraph.

Repressors are proteins which regulate gene expression, well described for bacteria and bacteriophages systems

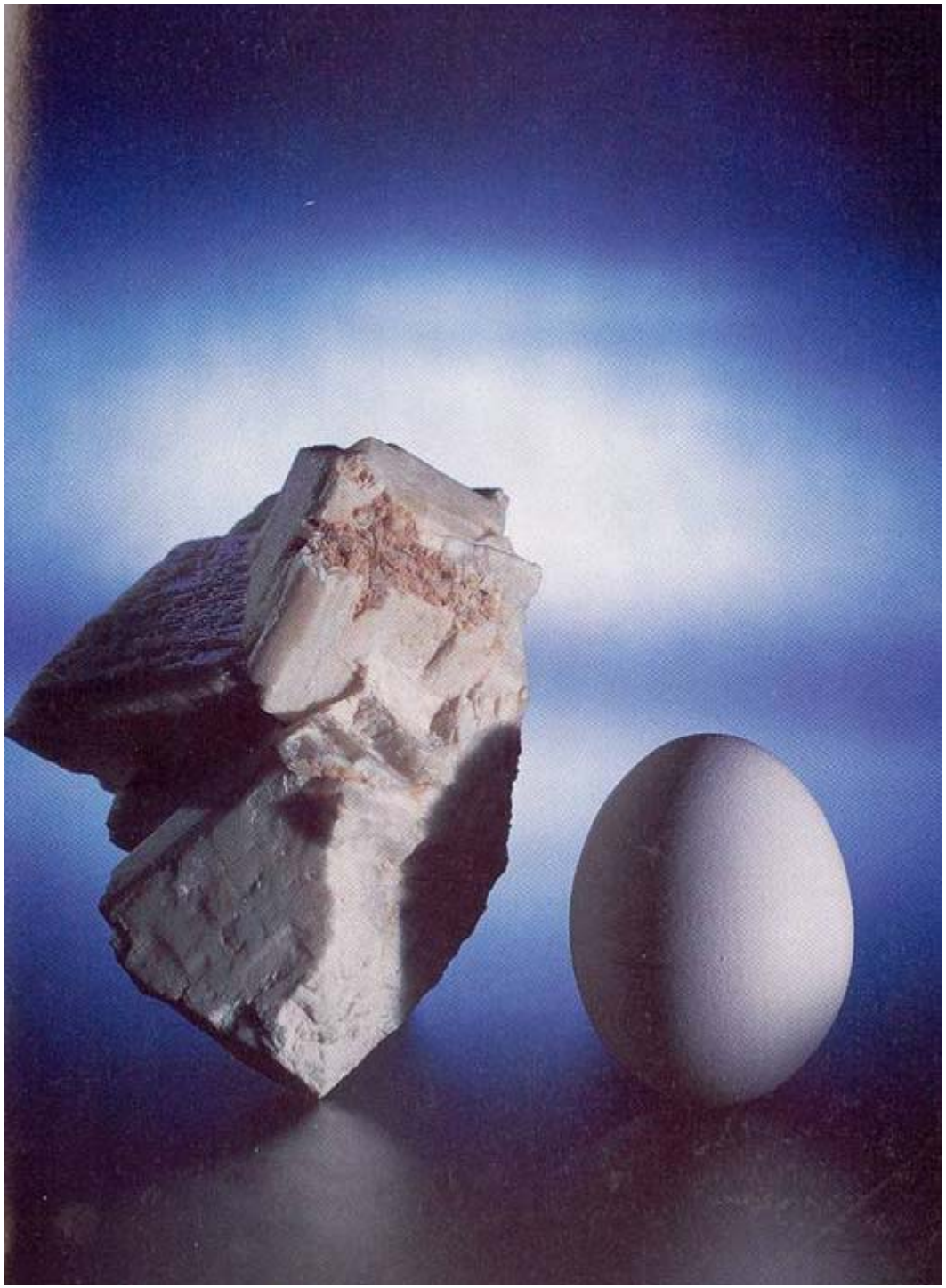
An explosive, concentration-dependent chain-extension reaction



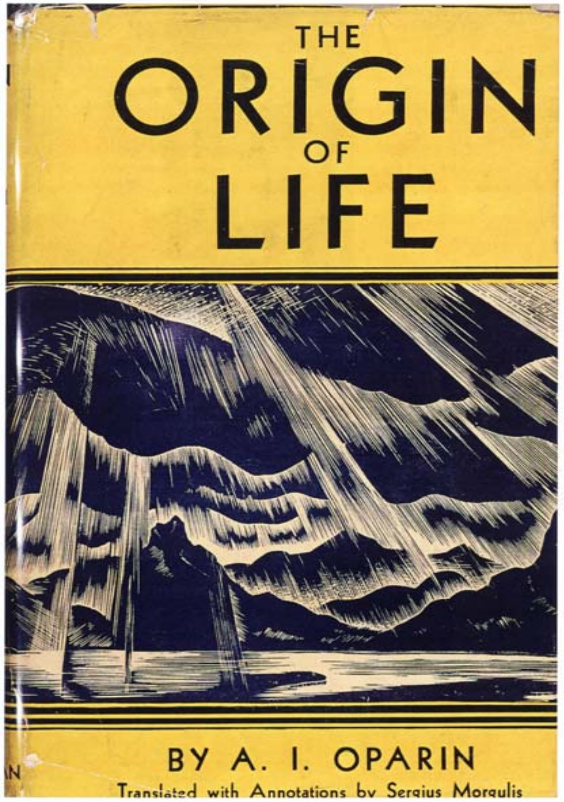
Louis Pasteur

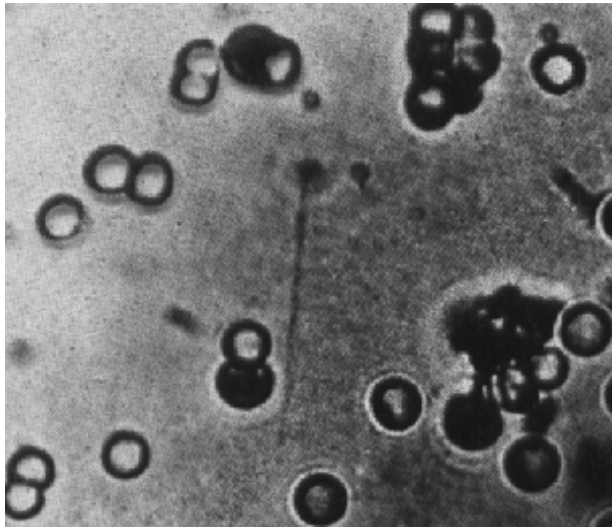


- **“*Omne vivum ex vivo*” (1864)**



Alexander I. Oparin





"*Proiskhozhdenie zhizny*" (The Origin of Life") 1924