Research on the origins of life: How to handle this problem?

Complex systems

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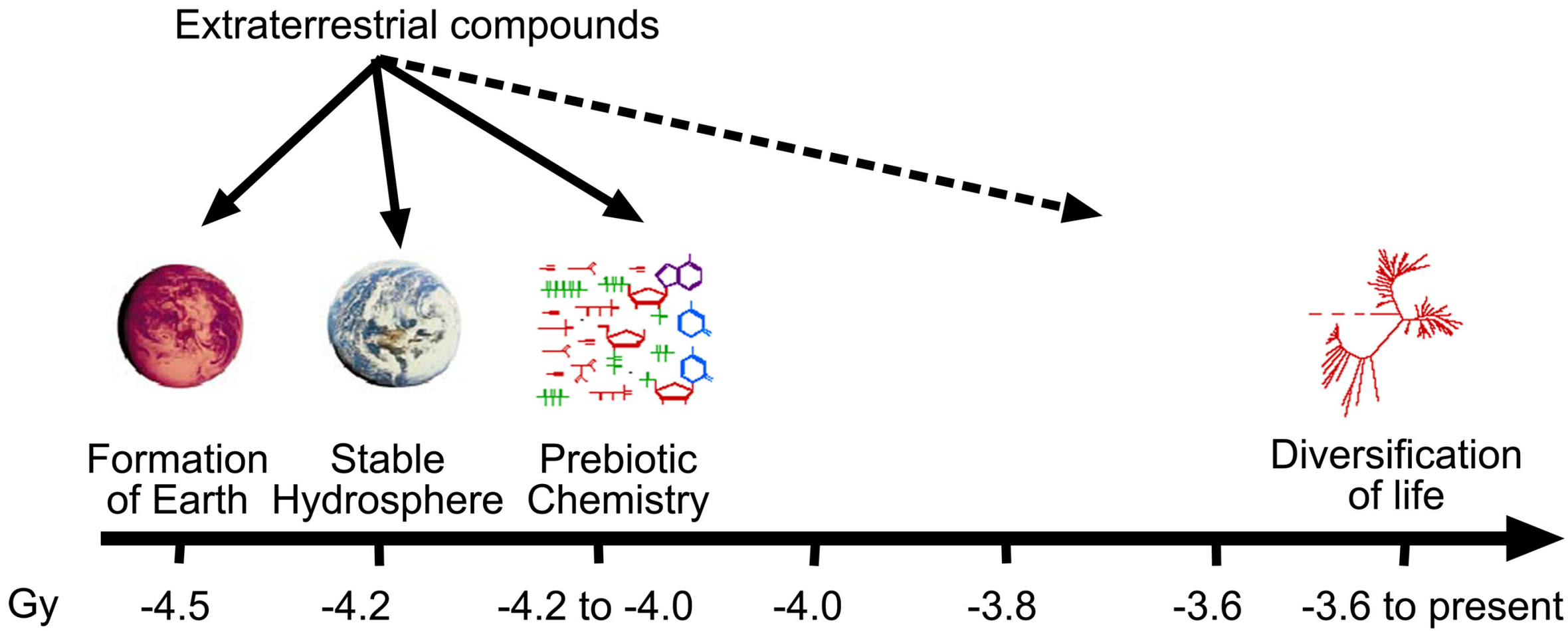
CERN, Geneva, May 20, 2011

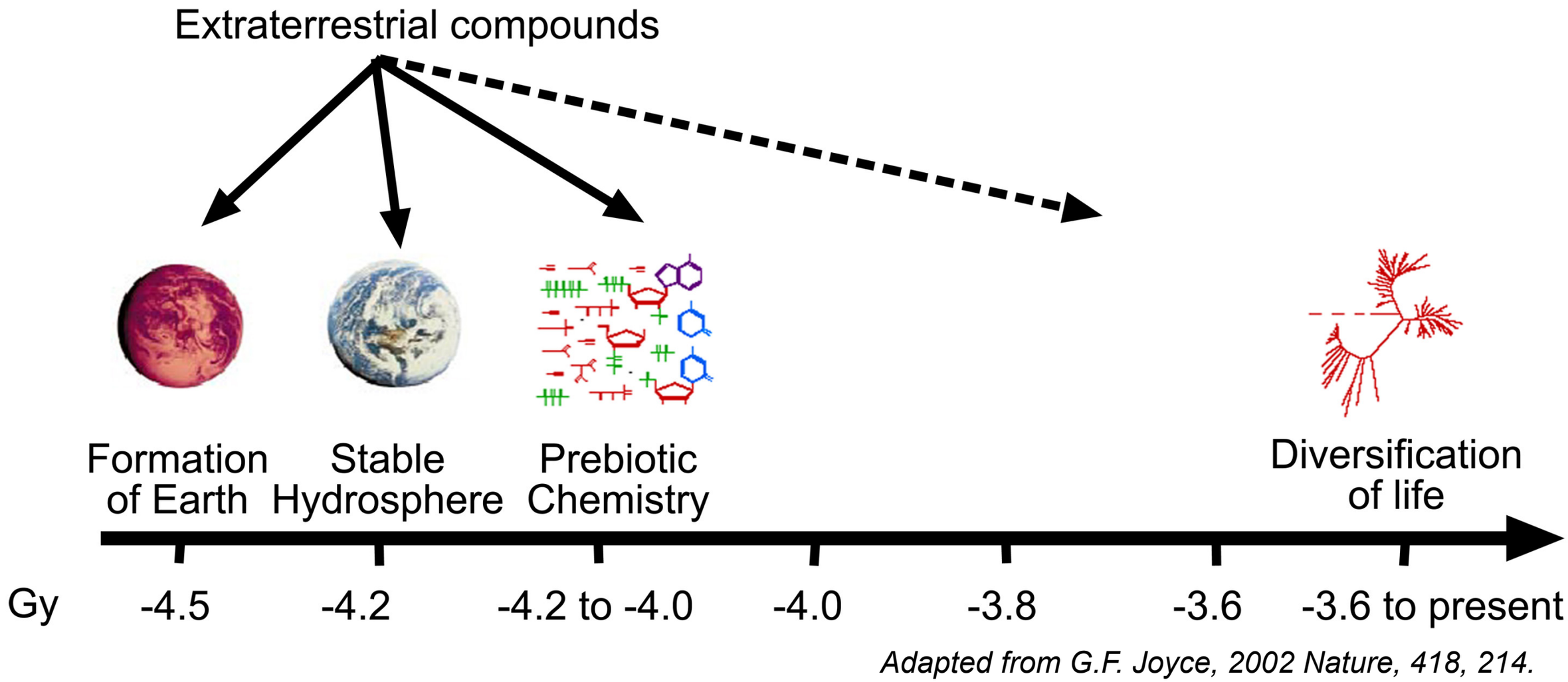
UNIVERSITY OF SOUTHERN DENMARK

Origins of Life: Scenario



Adapted from G.F. Joyce, 2002 Nature, 418, 214.

Origins of Life: Scenario



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LCA set was based on membranous container and the triad DNA-RNA-protein

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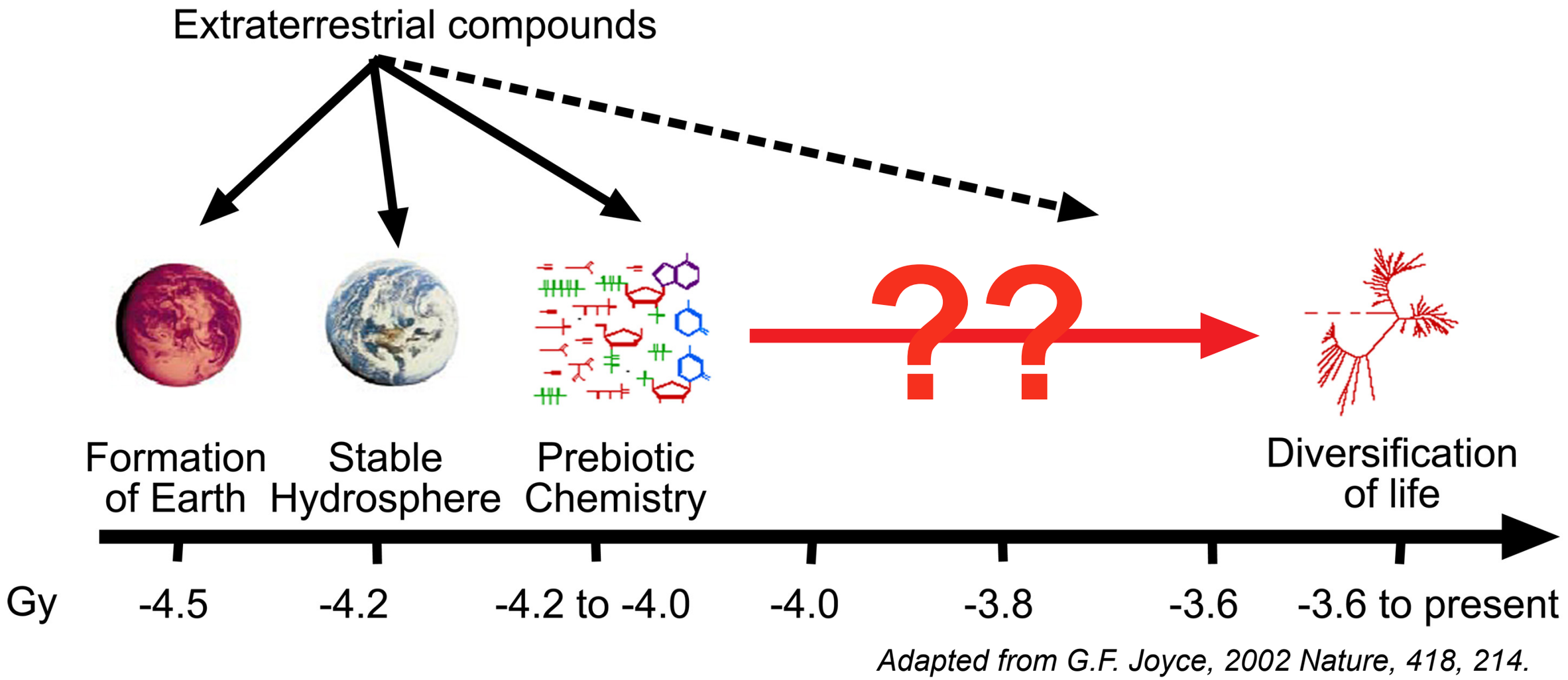

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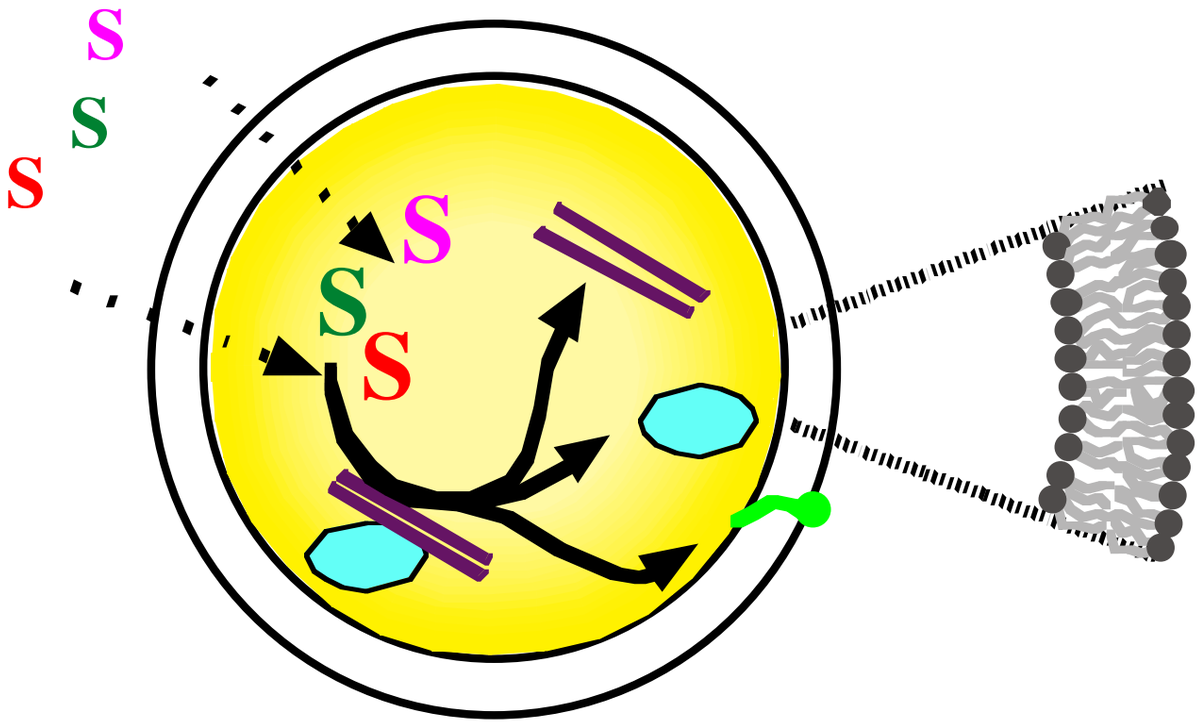
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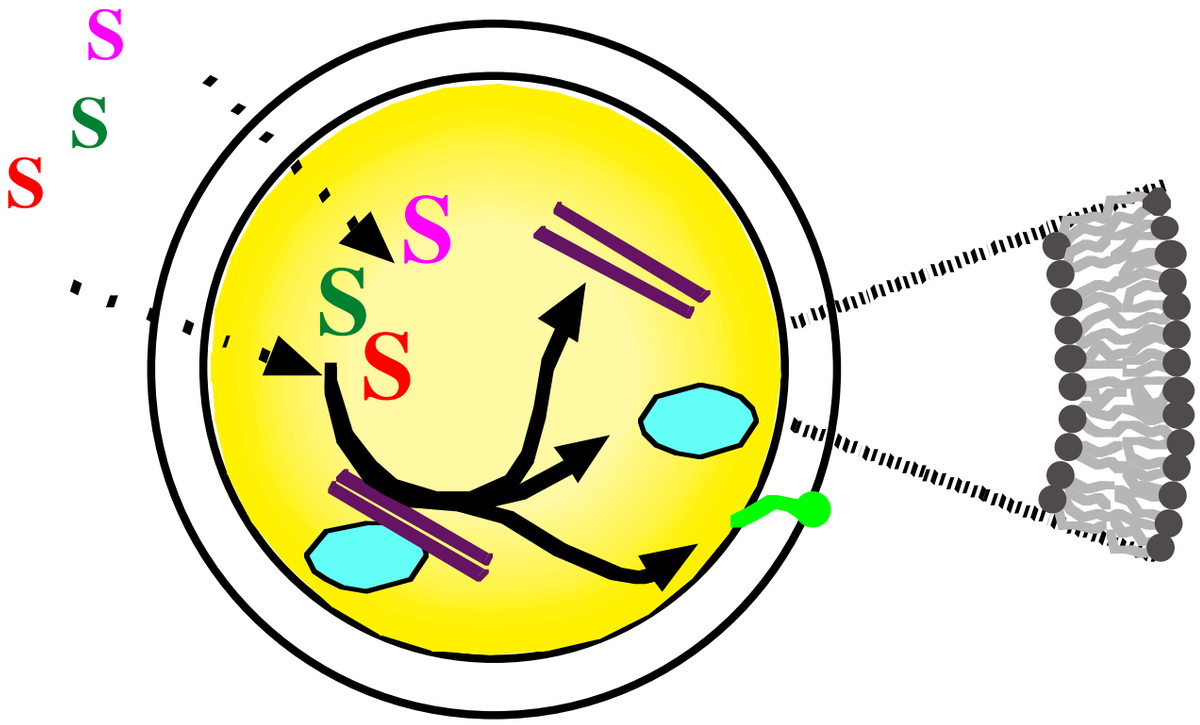
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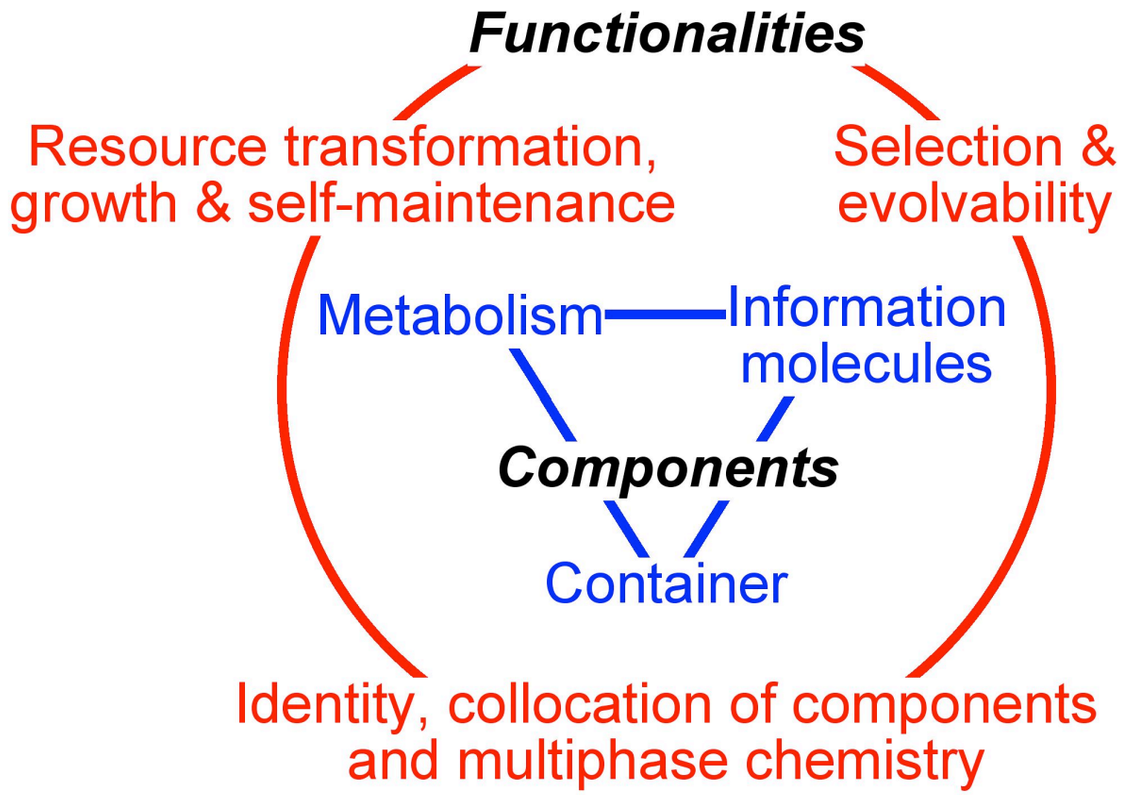
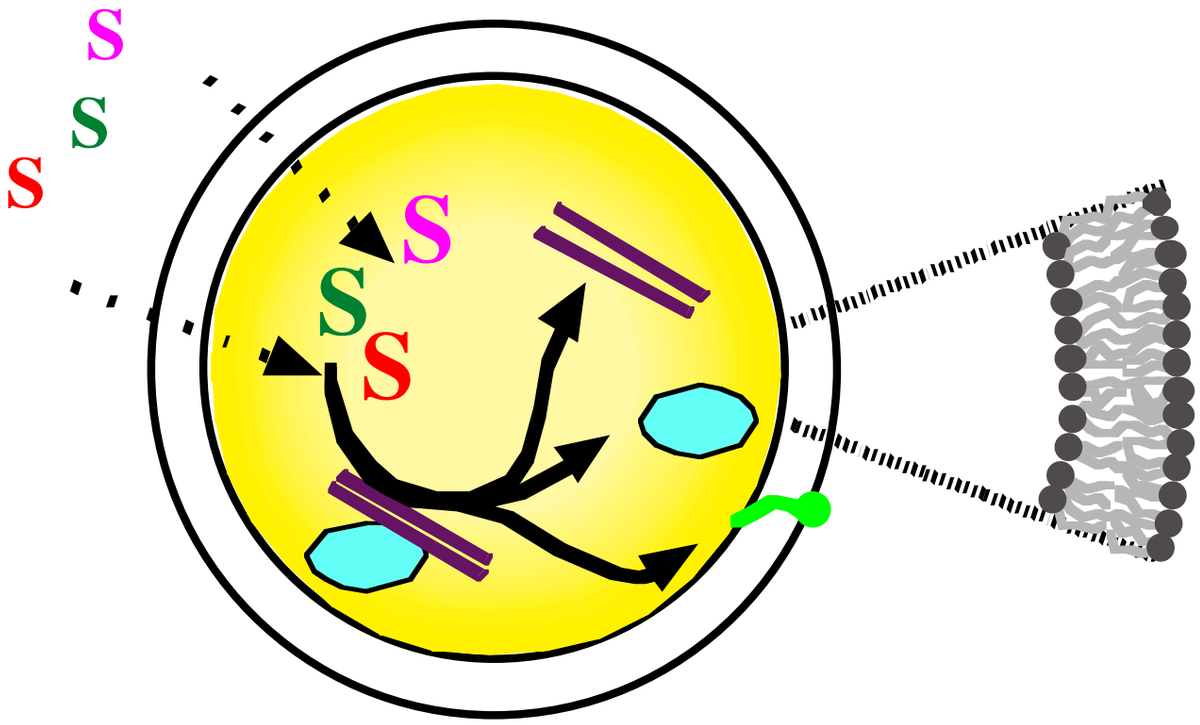
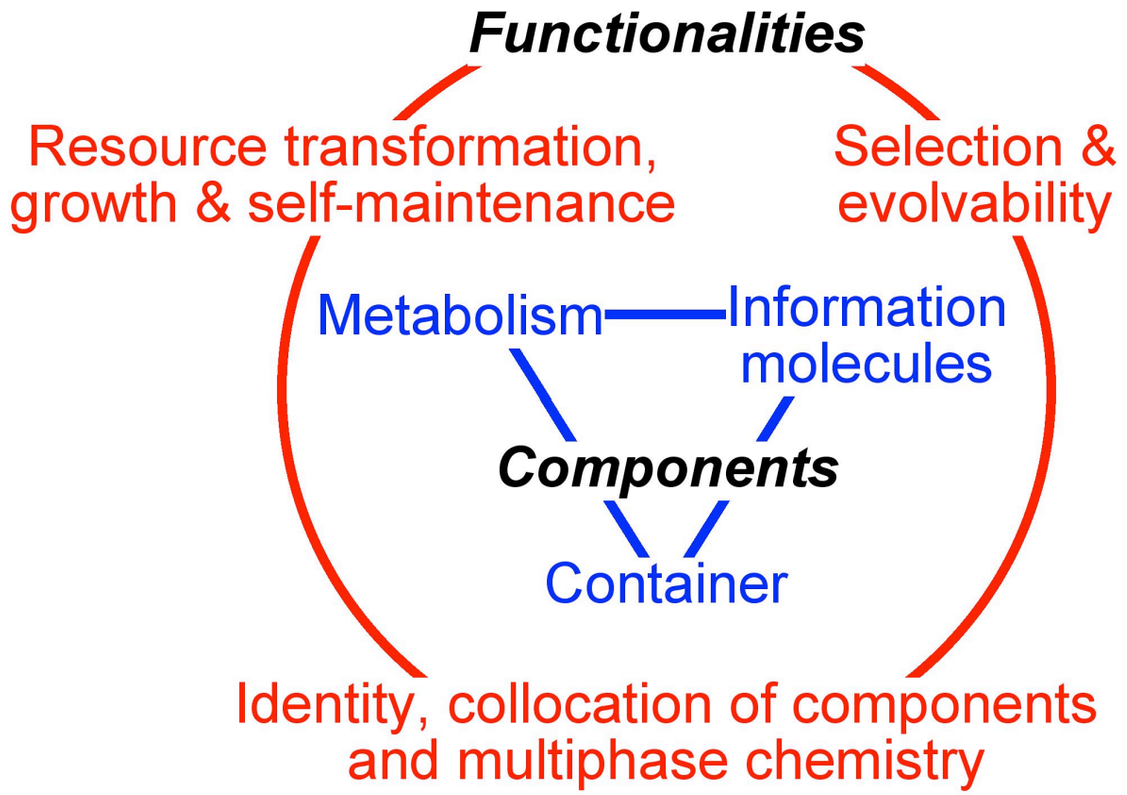
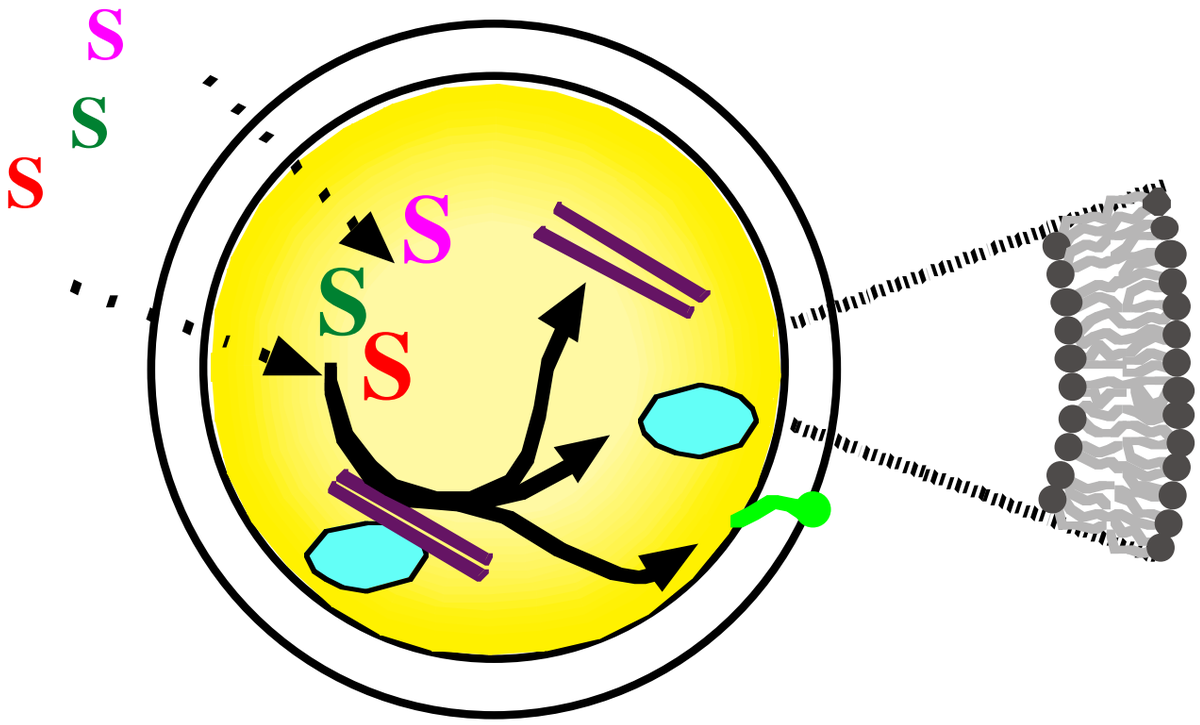
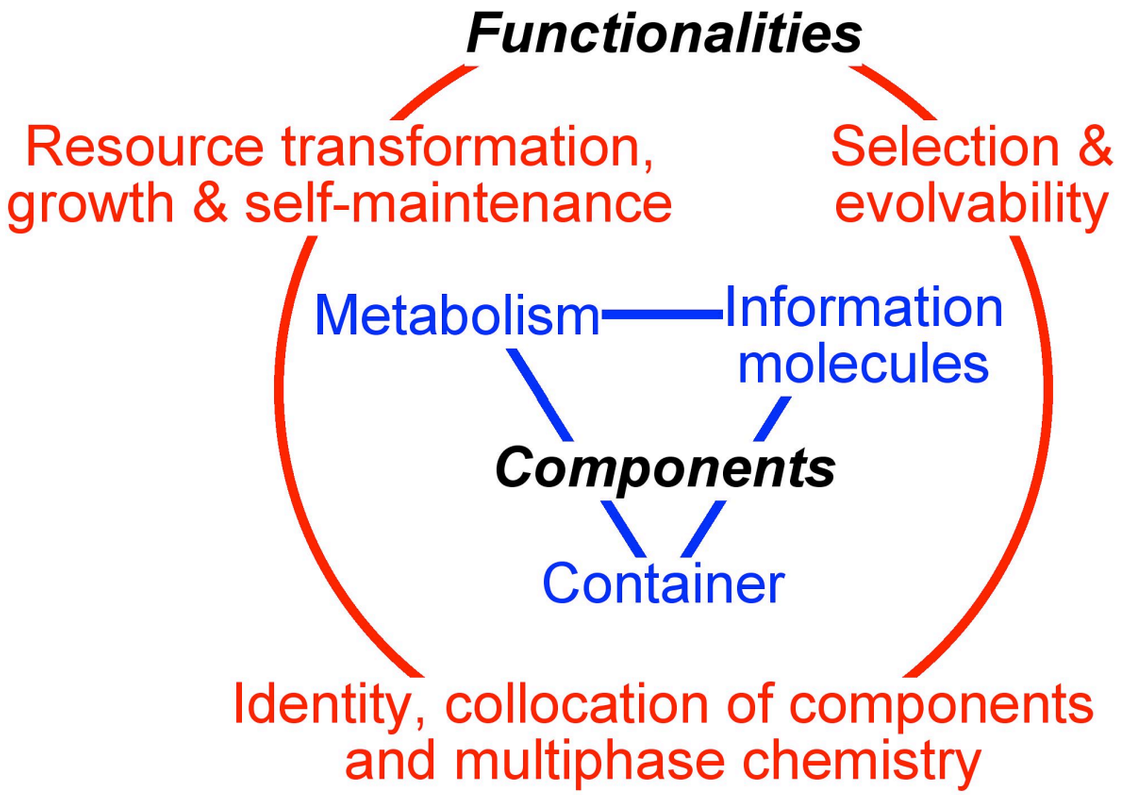

Functionalities
Resource transformation, growth & self-maintenance
Selection & evolvability
Metabolism
Information molecules
Components
Container
Identity, collocation of components and multiphase chemistry





Self-maintenance ***(Resource transformation, identity preservation)***
Self-replication ***(Growth and division)***
Evolution ***(Trait selection)***





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In the systemic approach to building a minimal self-replicating chemical system, only a system composed of these three components can mimics the systemic and functional properties of living systems

Protocell concept: Components (bottom-up approach)

Metabolism

Container

Information

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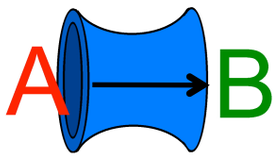
Metabolism



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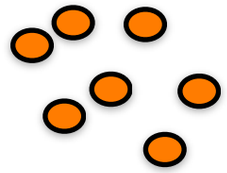

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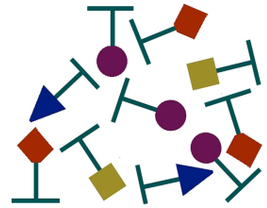

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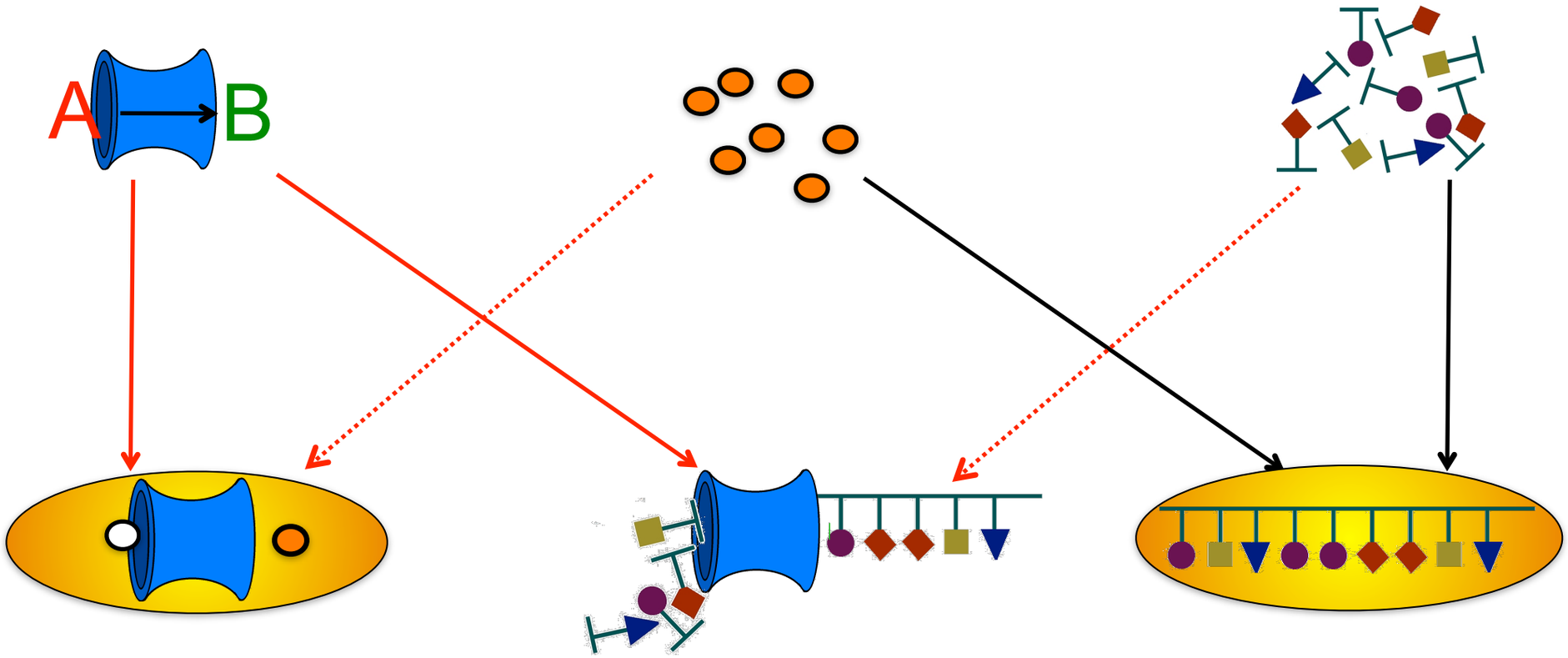

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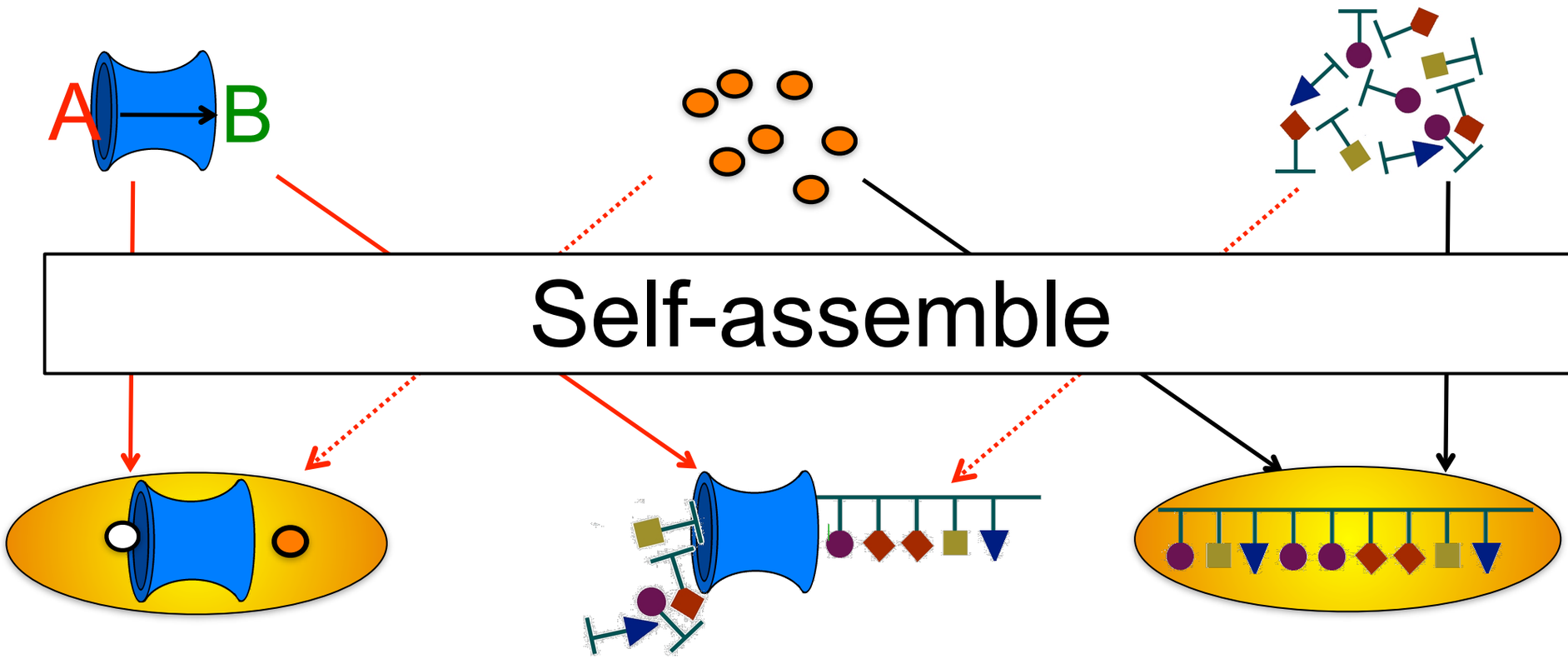

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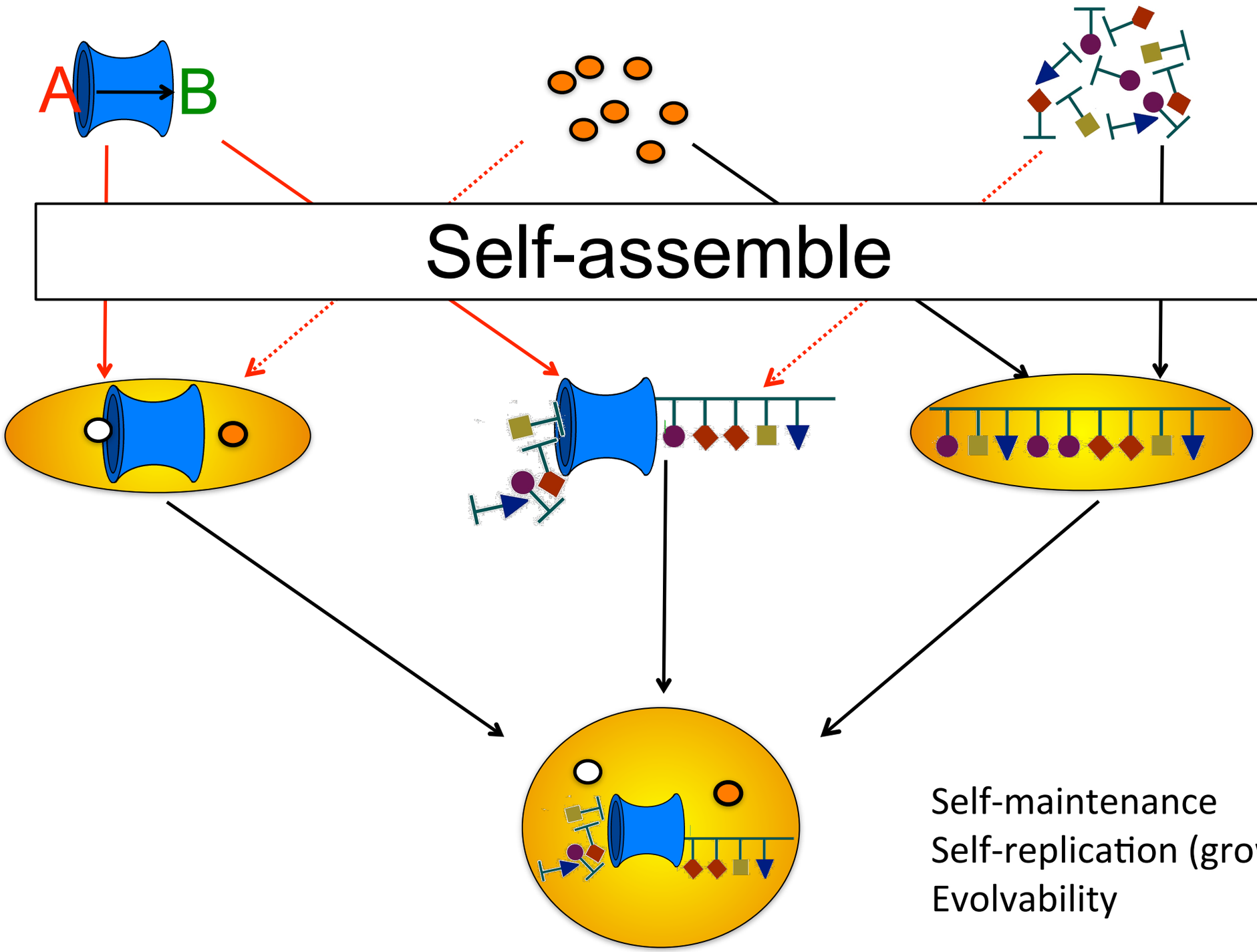

Self-maintenance
Self-replication (growth and division)
Evolvability

Protocell concept: Components (bottom-up approach)

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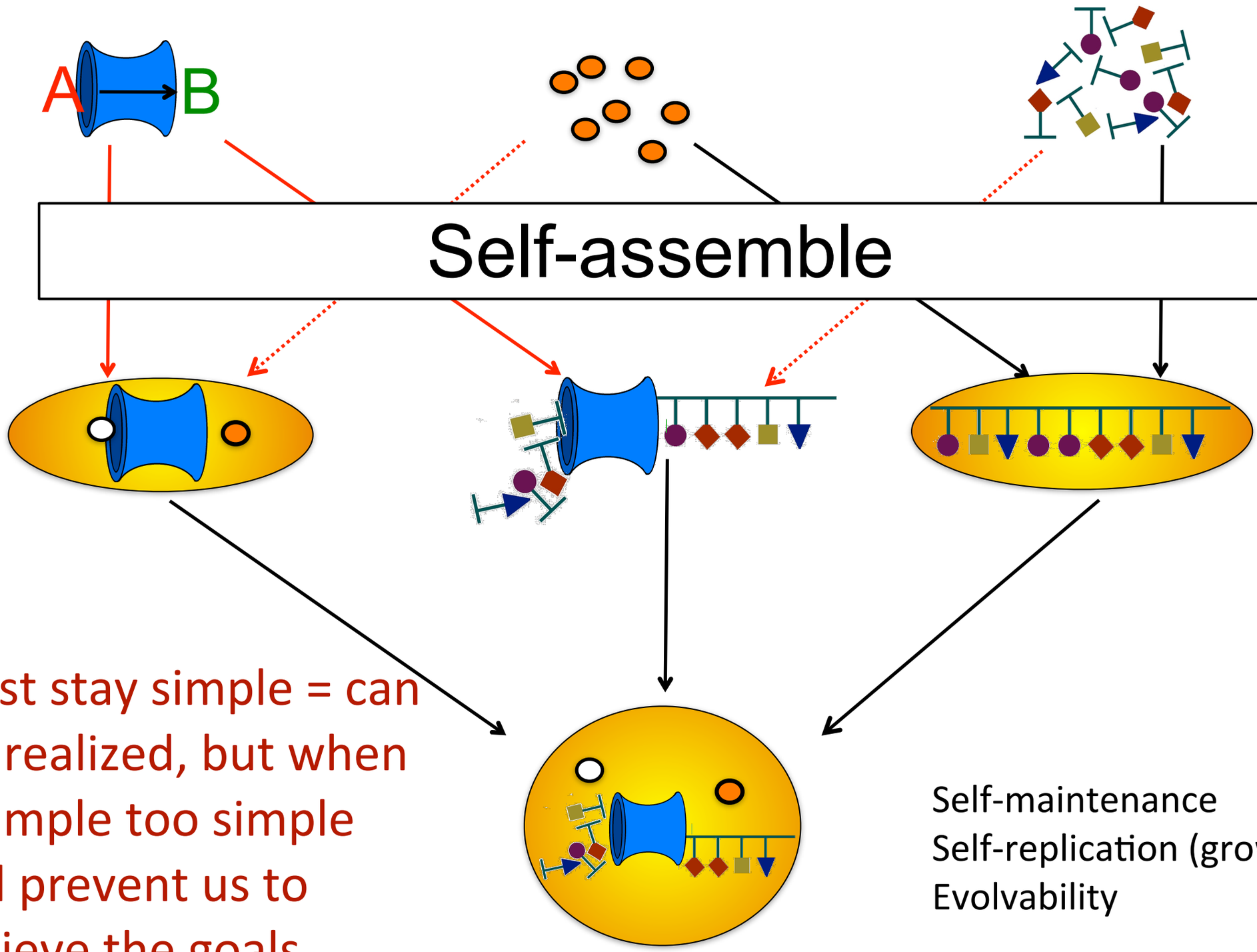

Must stay simple = can be realized, but when is simple too simple and prevent us to achieve the goals.

Self-maintenance
Self-replication (growth and division)
Evolvability

Primitive membranous compartments: Self-assembly of prebiotically plausible amphiphiles

Mixture of various single chain amphiphiles (chain length, headgroup functions and numbers)

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Environmental impacts on single-chain amphiphile membranes

- pH *(Apel et al 2002 Biochim. Biophys. Acta)*
- Dilution (CVC) *(Maurer et al 2009 Astrobiology)*
- Salinity (*Monnard et al 2002 Astrobiology*)
- Temperature (*Mansy & Szostak 2008 PNAS, Maurer et al 2009 Astrobiology*)

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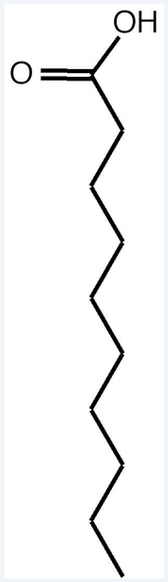
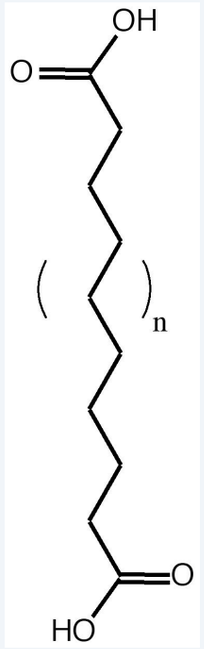
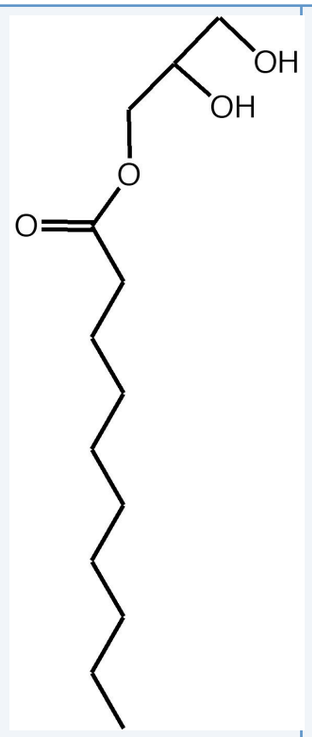
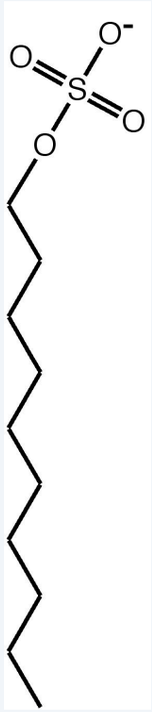
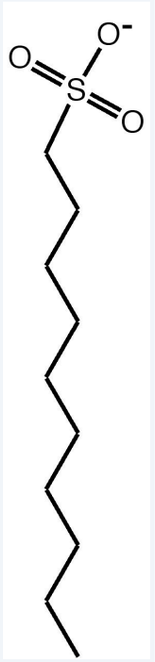
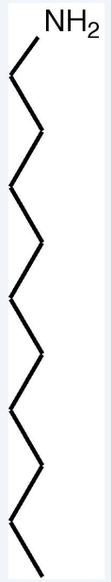
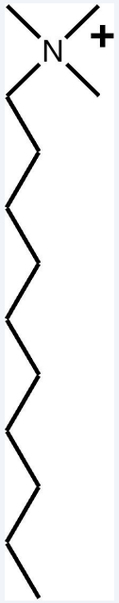
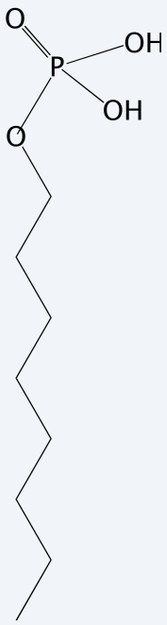
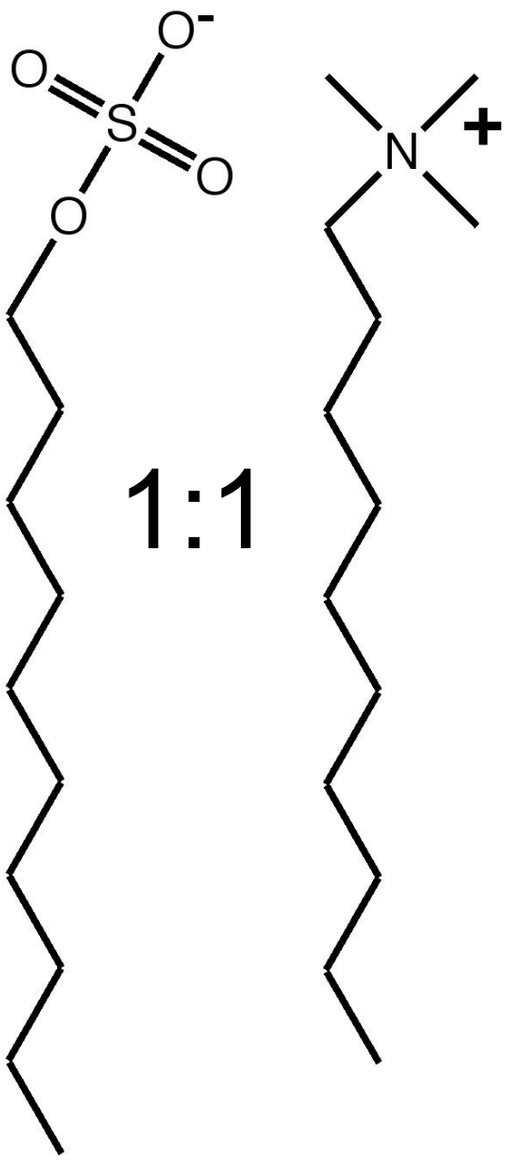
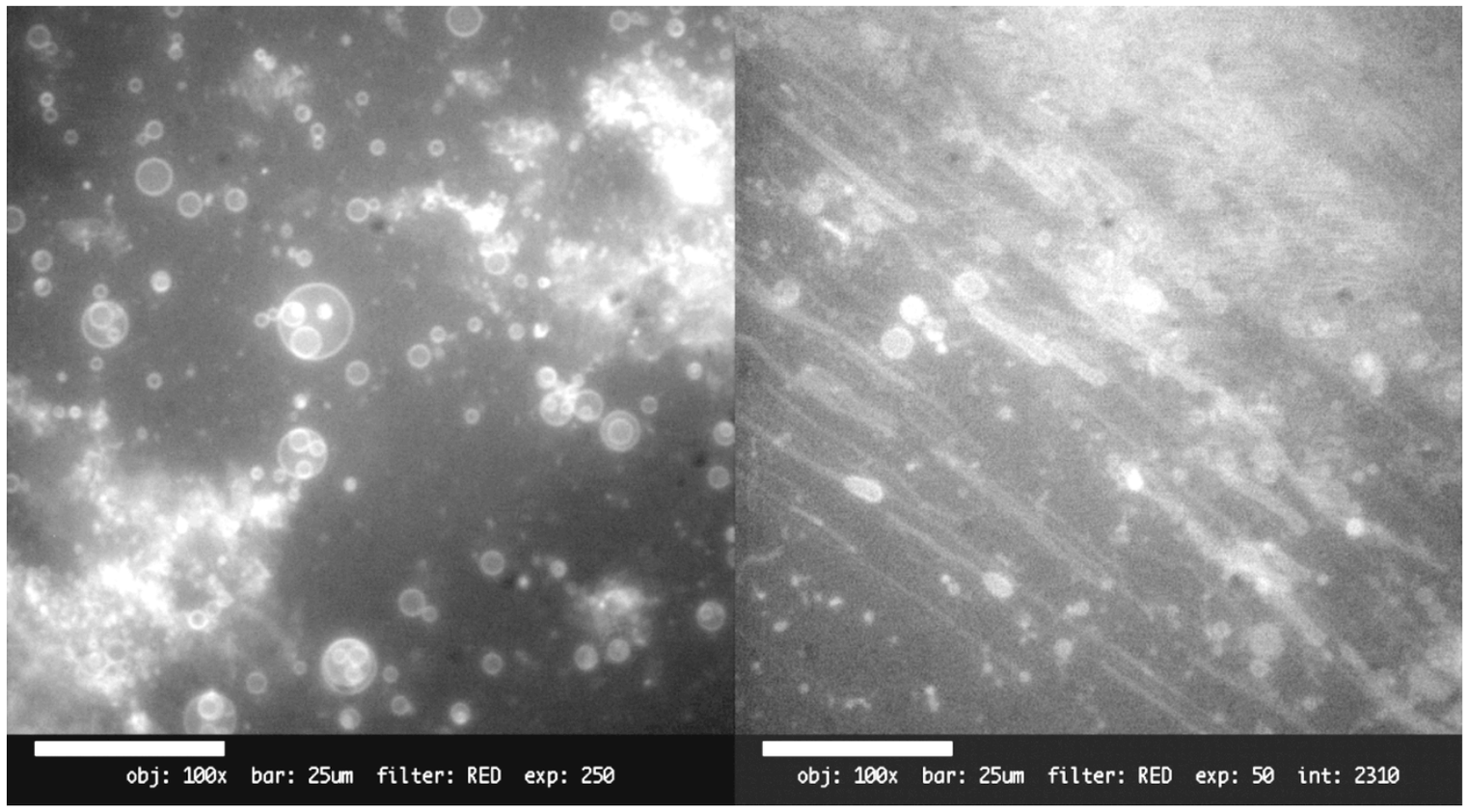
Fluctuations in these parameters occurred frequently

Chemical structures

									
Headgroup	COOH	OH	Di COOH (bola)	Glycerol-ester	SO_4^-	SO_3^-	NH_2	$N(CH_3)_3^+$	PO_4^{2-}
In Chondrites	☺	☺	☺	?	?	?	😐	😐	?
Prebiotic synthesis	☺	☺	?	☺	?	?	?	?	☺

Mixtures of single chain amphiphiles that do not form membranous structures on their own

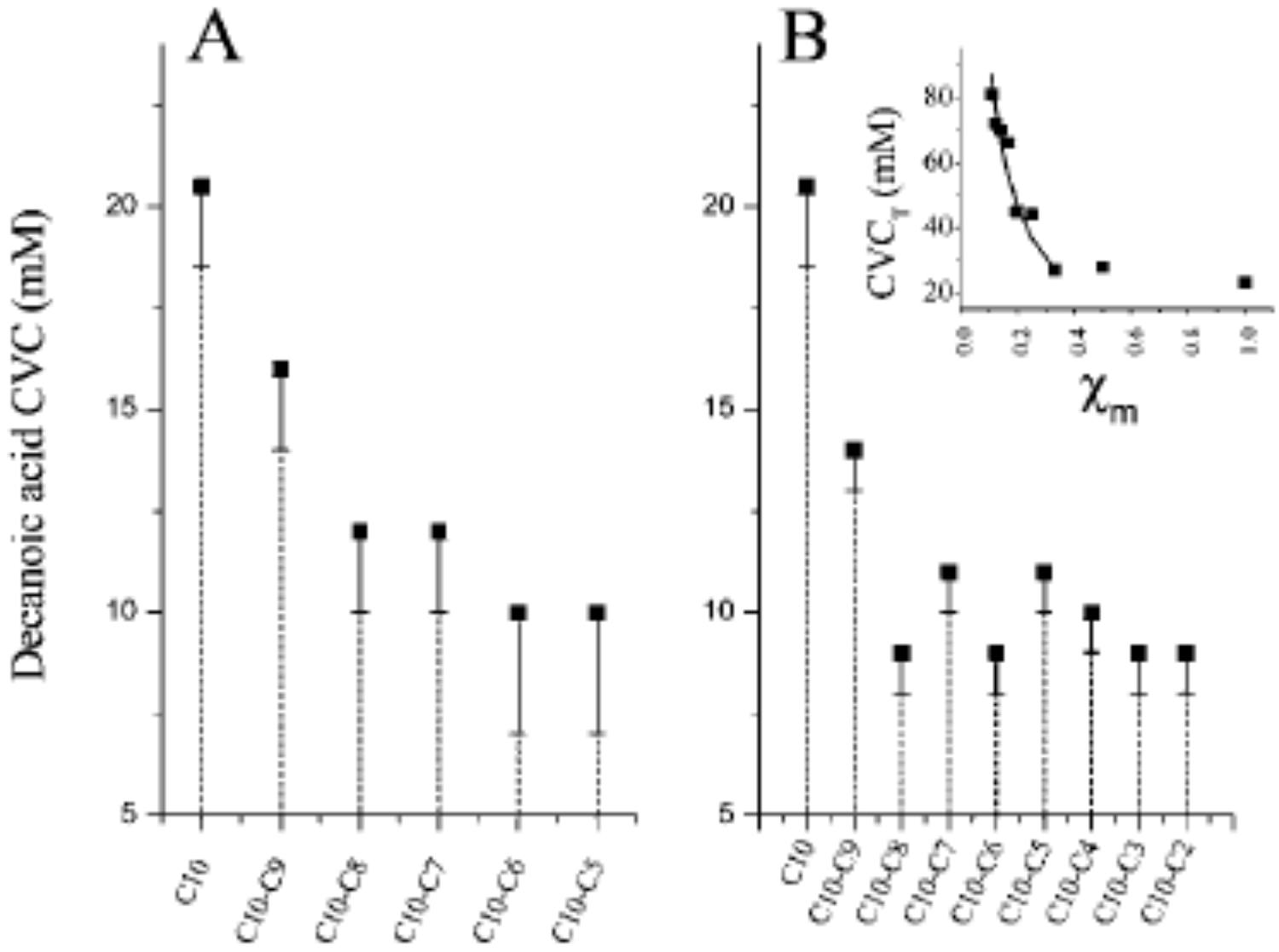




pH = 11.0 to 3.0

T.E. Rasmussen

More complex mixtures:
Prebiotically plausible mixture of carboxylic acids

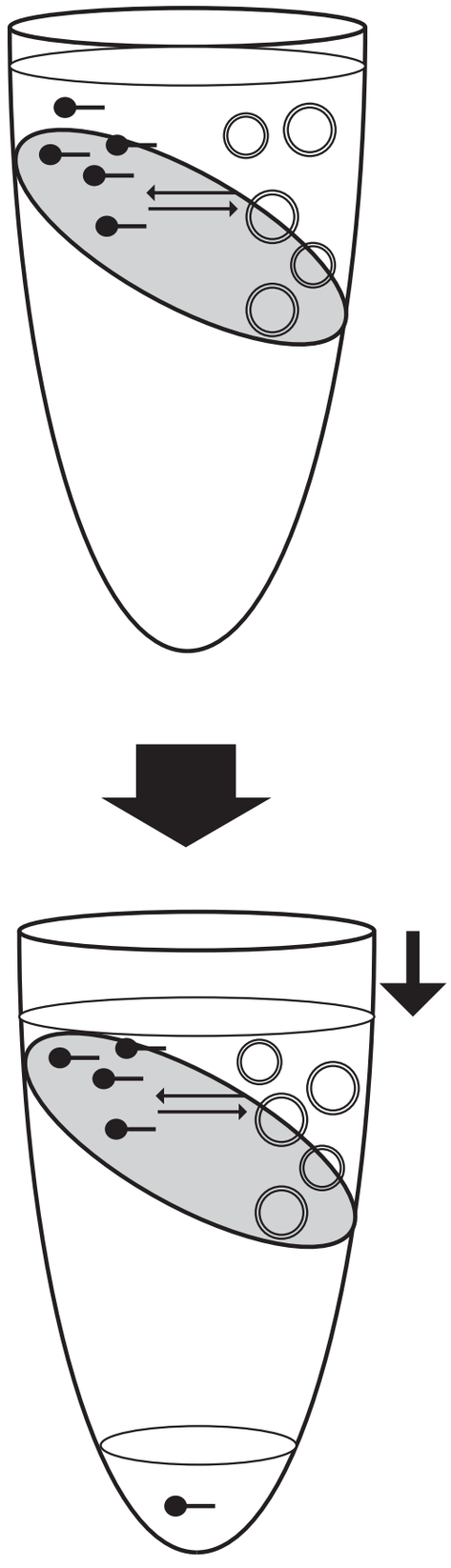


pH= 7.25 ± 0.05

A) CVC_{DA} in mixtures of constant concentration of the other CAs

B) CVC_{DA} in mixtures were all CA concentration ratio are maintained

Cape et al., 2011 Chem Sci



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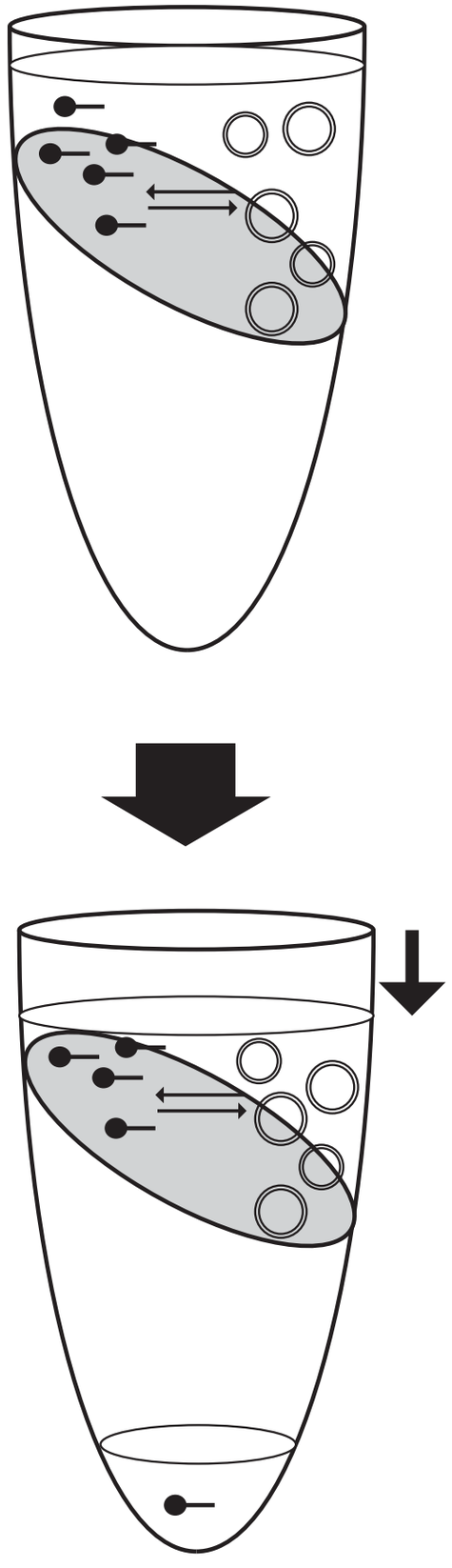
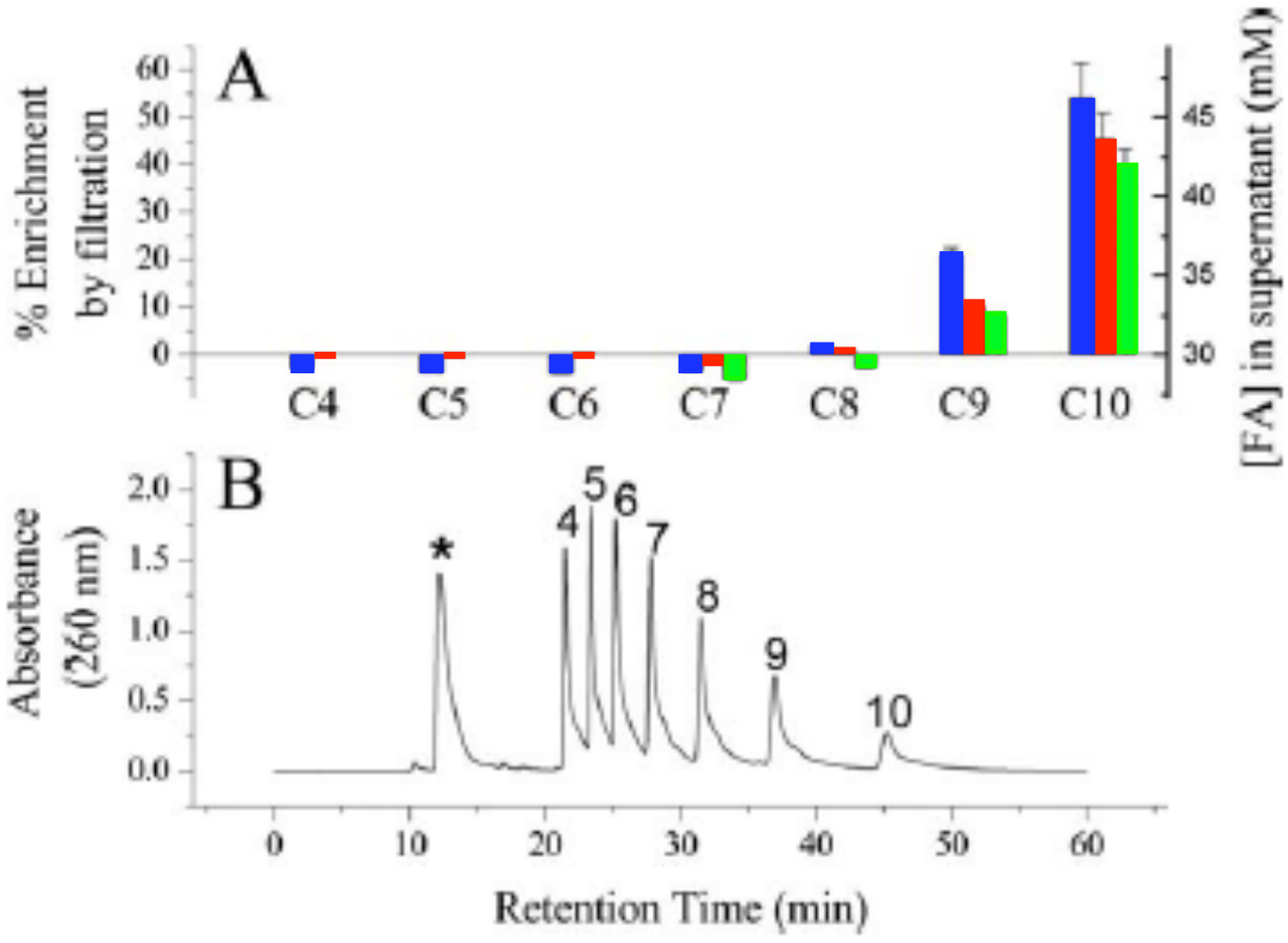


Mixture containing C7 to C10

Mixture containing C5 to C10

Mixture containing C4 to C10



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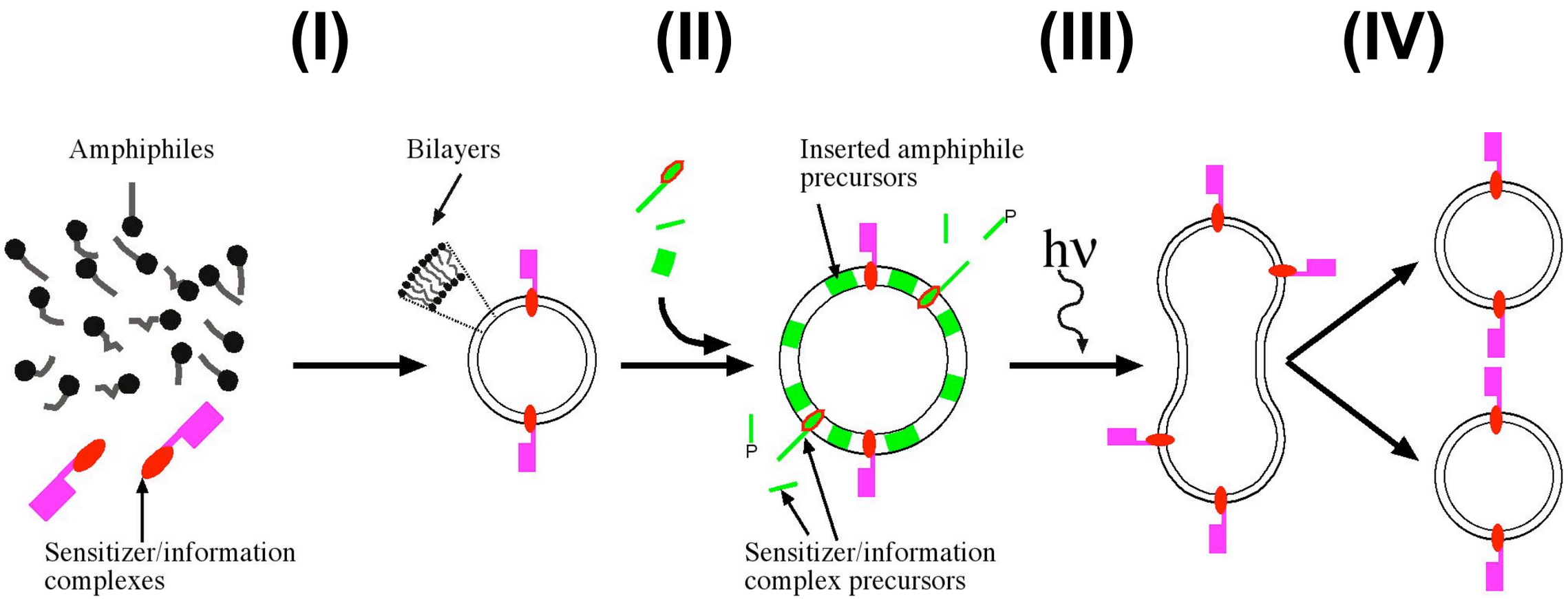
Protocell Assembly: a bottom-up systemic approach



Traits specific to this design

- Container is the amphiphile structure itself

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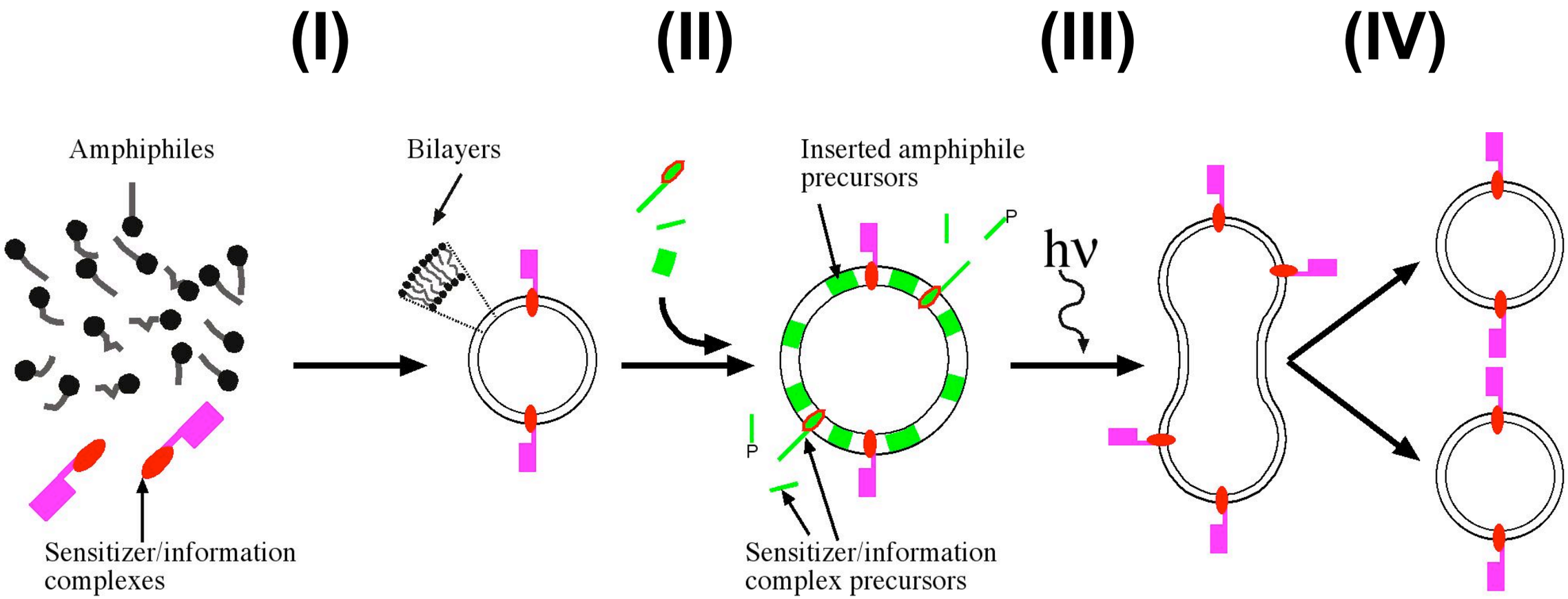

Traits specific to this design

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- Total self-assembly of initial protocell

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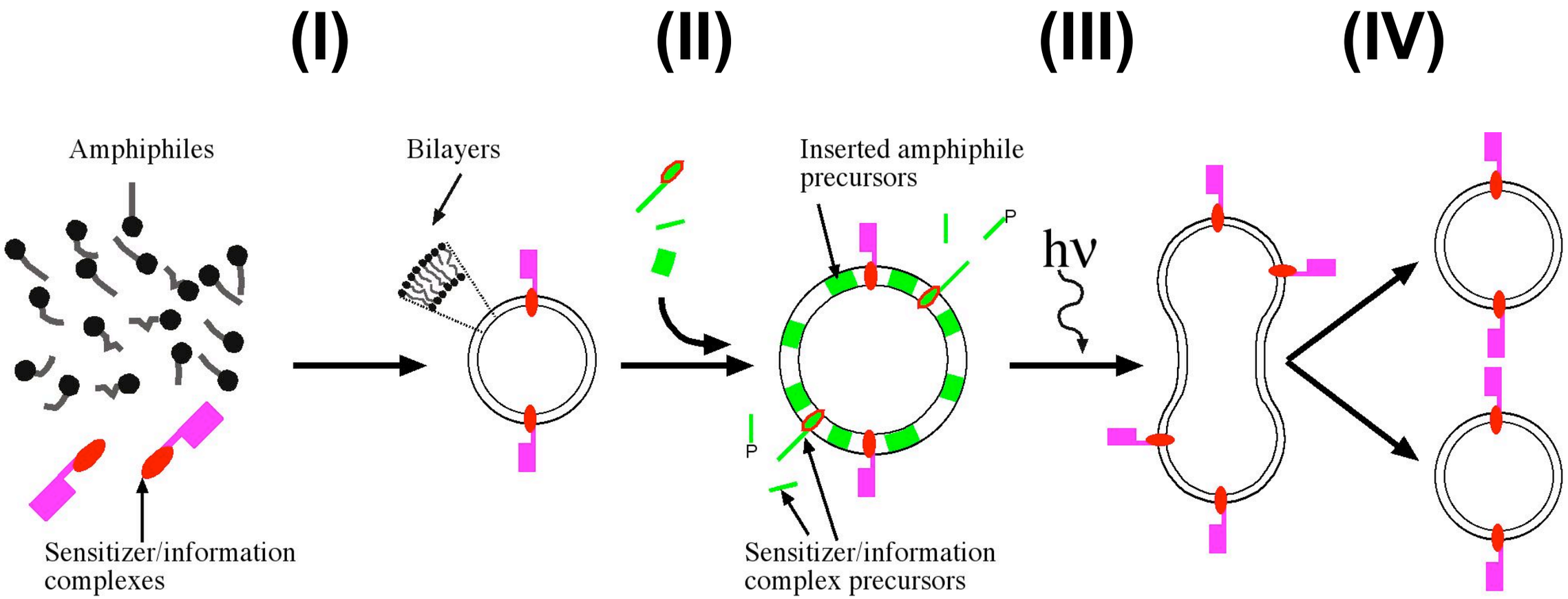

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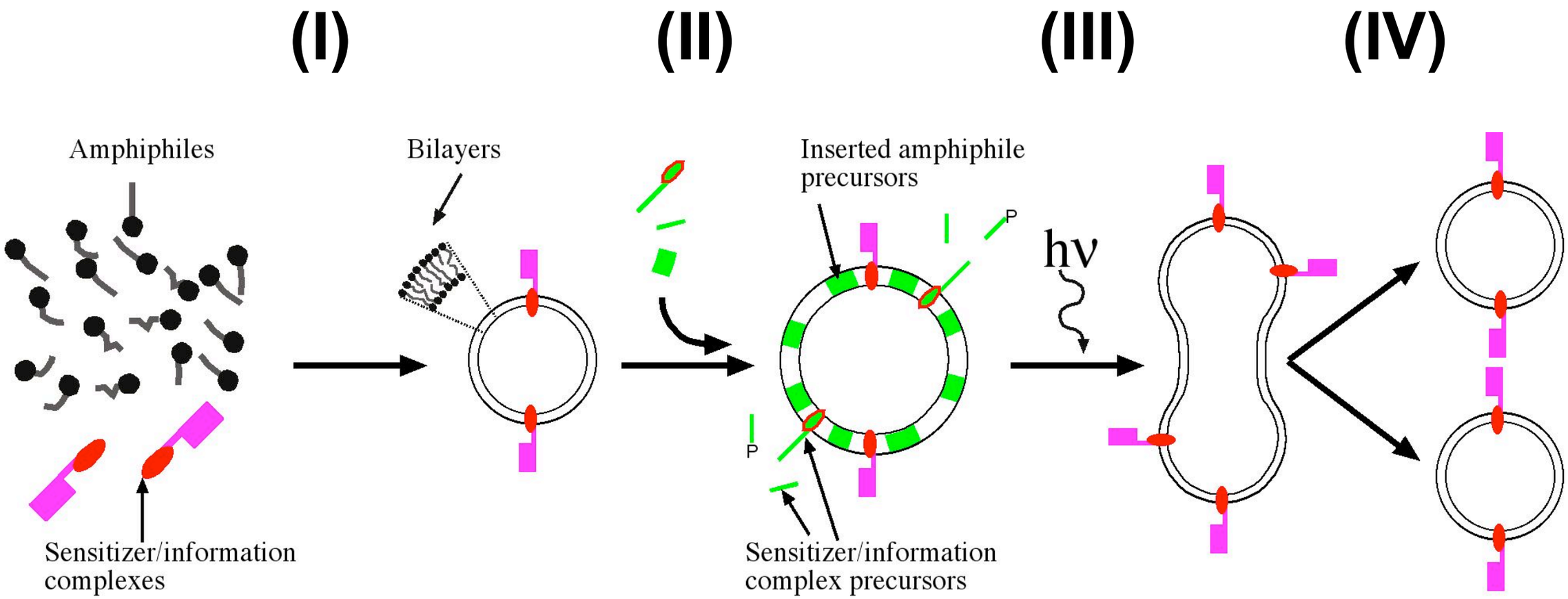

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- Coupling of catalytic reaction to uptake of primary energy (light)

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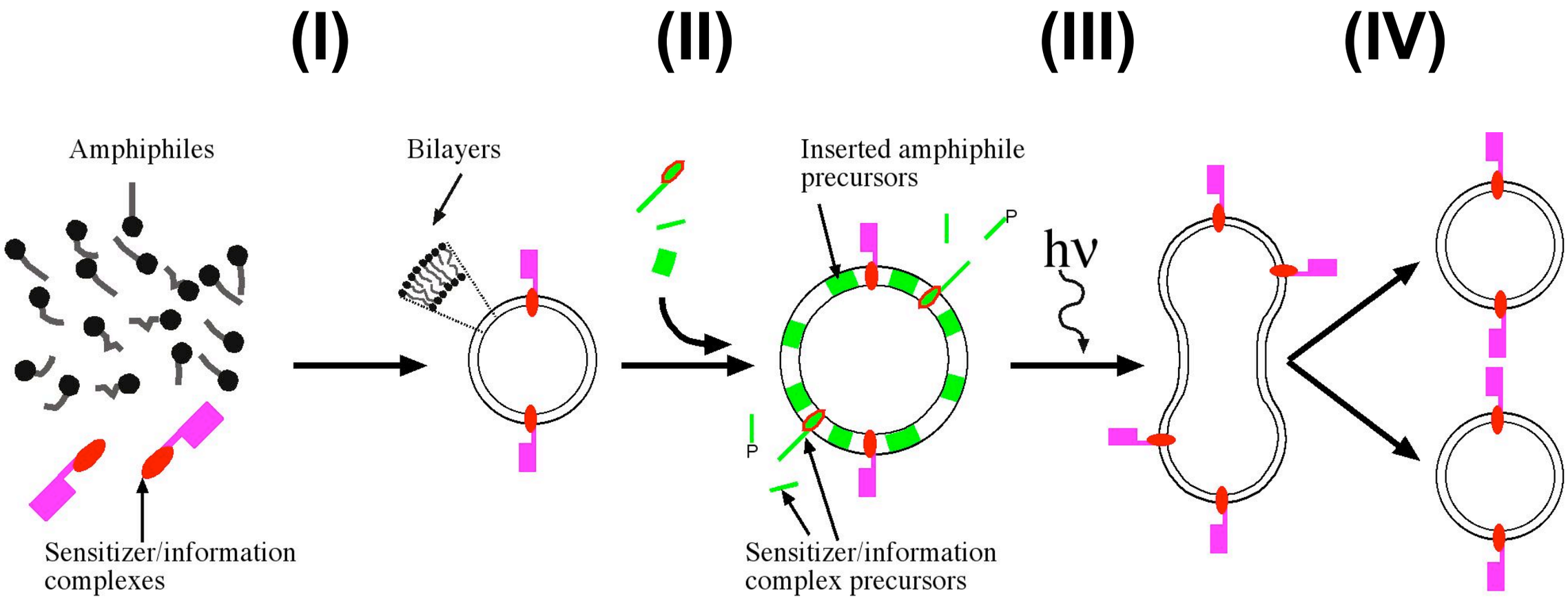

Traits specific to this design

- Container is the amphiphile structure itself
- Total self-assembly of initial protocell
- Direct assess to “nutrients
- Coupling of catalytic reaction to uptake of primary energy (light)
- Direct control of the catalysis by the “information”

Possible information control of metabolism

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DNA as conducting polymer

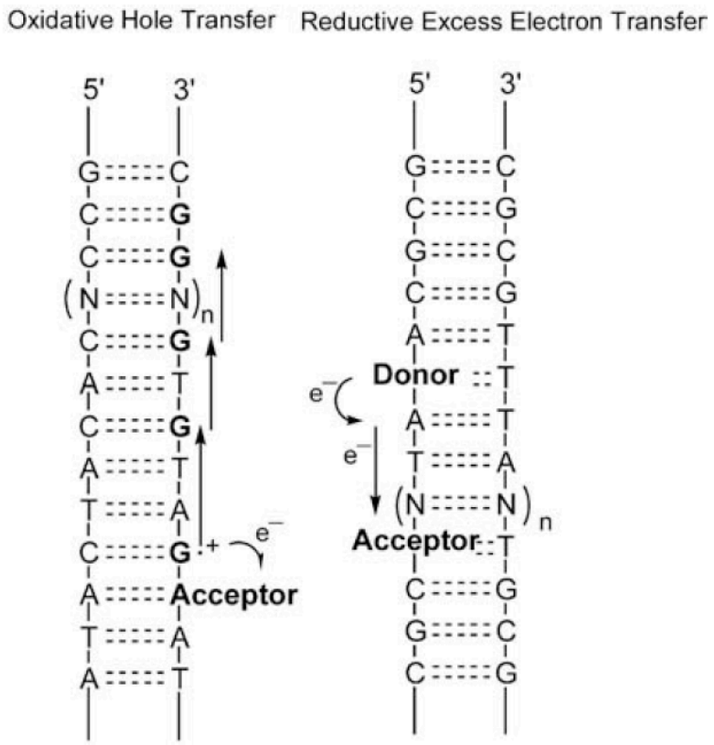

Fig. 1 Oxidative transfer of a radical cation through DNA and reductive transfer of an excess electron through DNA

Behrens, C. et al 2004 Top. Curr. Chem

In Principle DNA could be an actuator for Redox or photochemical reaction even in small double stranded oligomeric systems

Possible information control of metabolism

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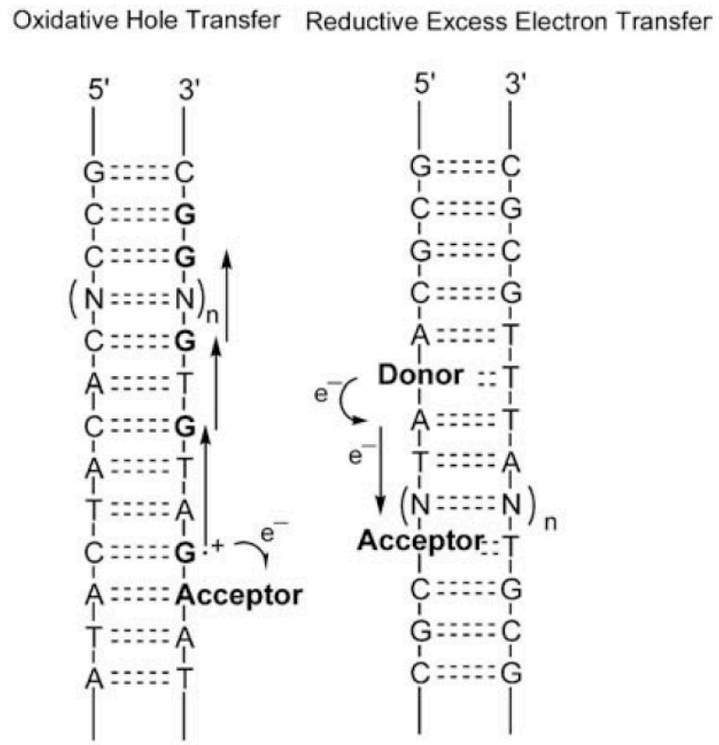

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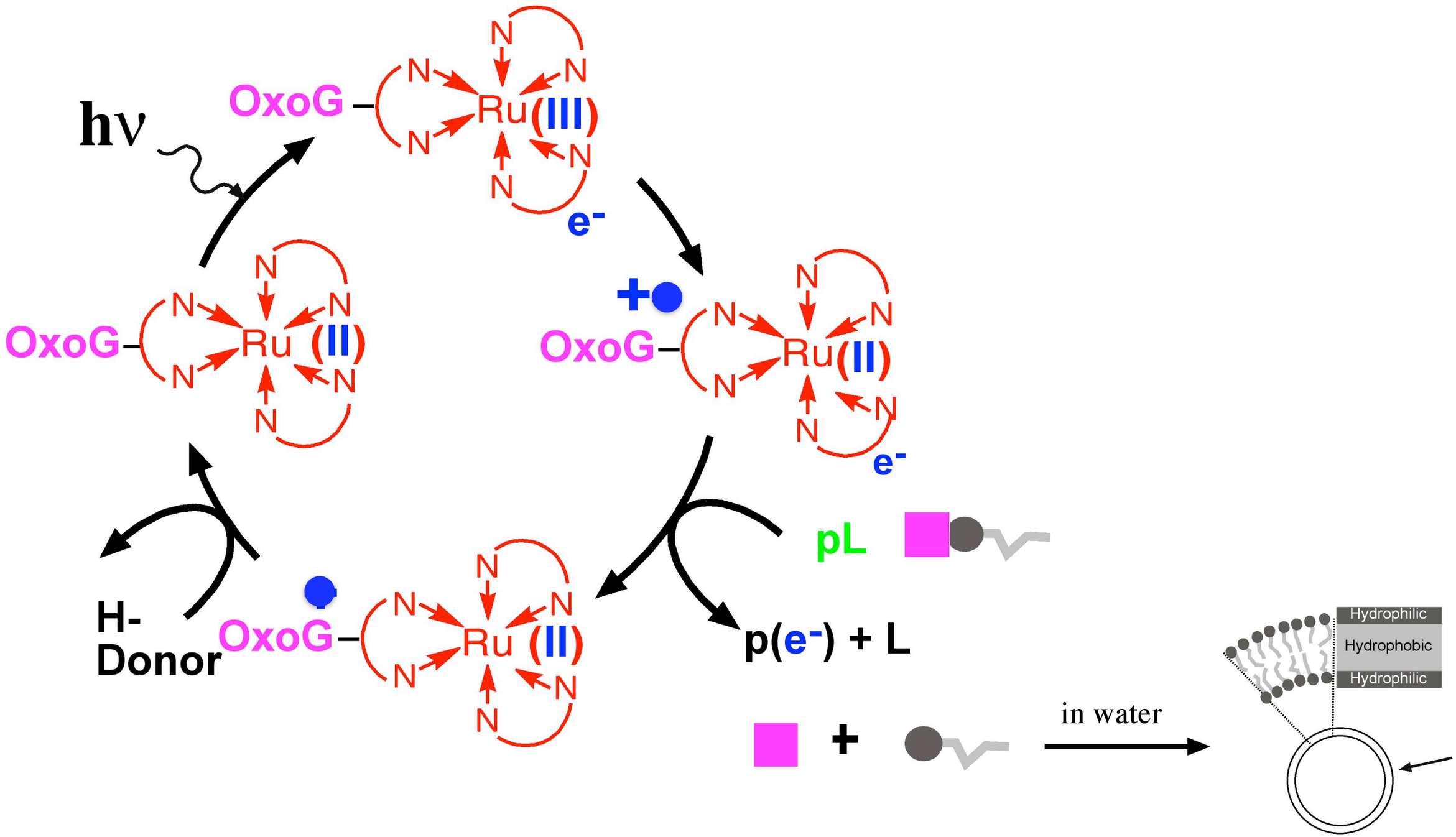
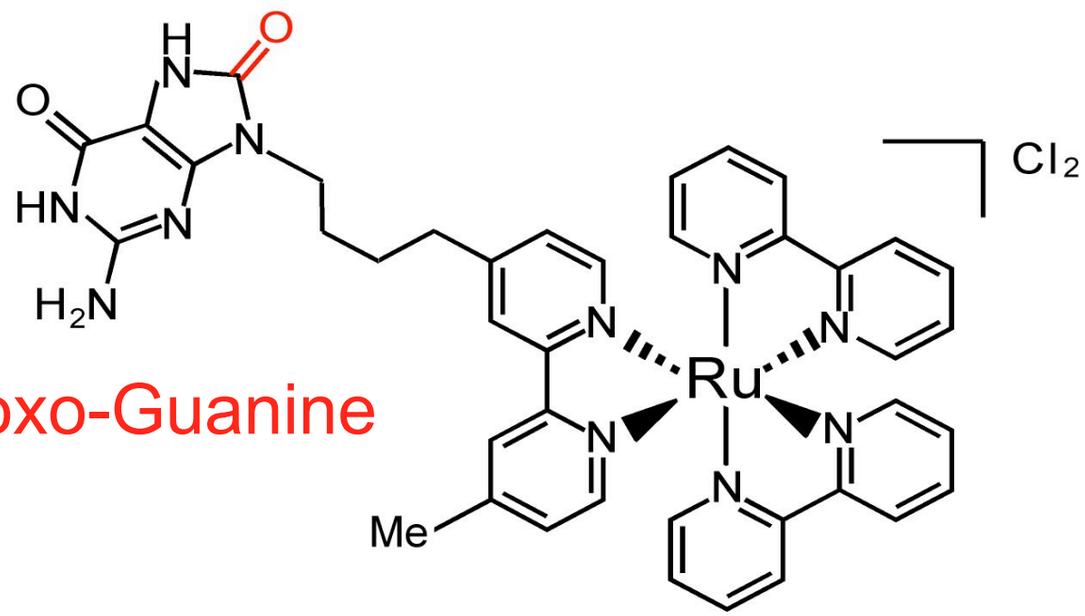
two problems

- degradation of DNA
- electron relay must be recycled

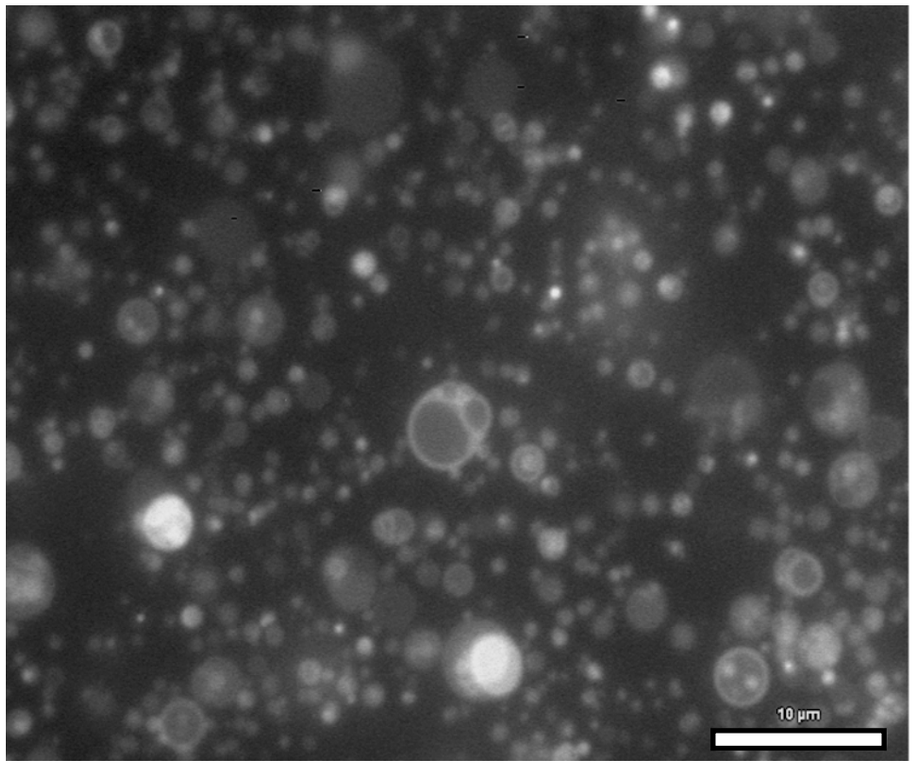
Conclusion: Protocell Assembly: “Info”-Metabolism-Container Interconnection



Impact of the “information” molecule



8-oxo-Guanine



Membranous structures (100%)

Declue et al 2009 JACS

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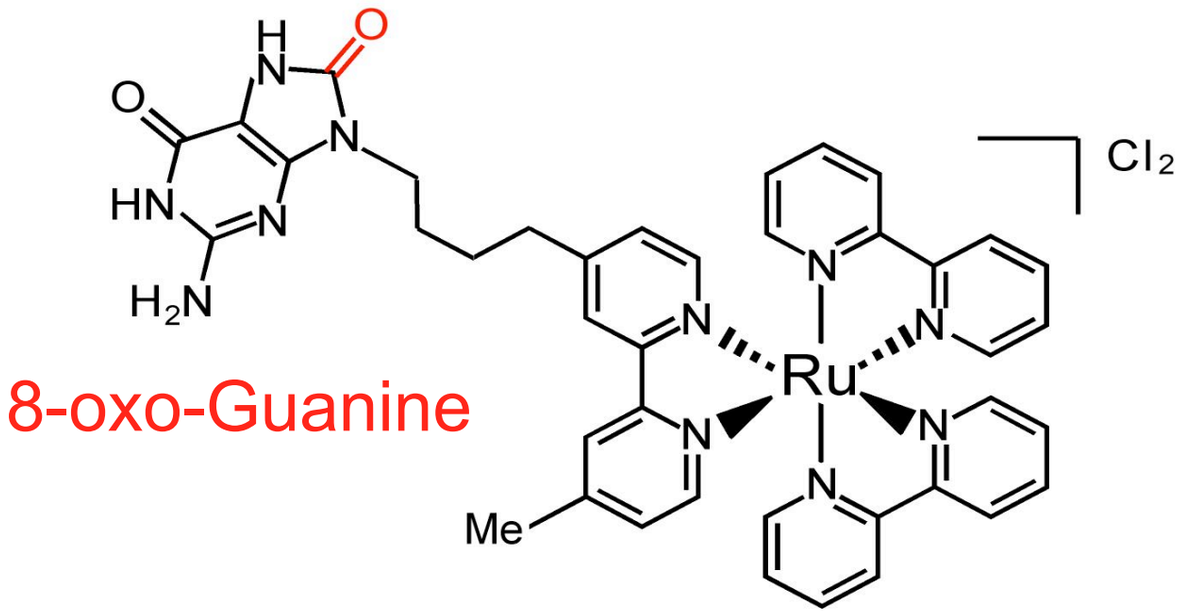

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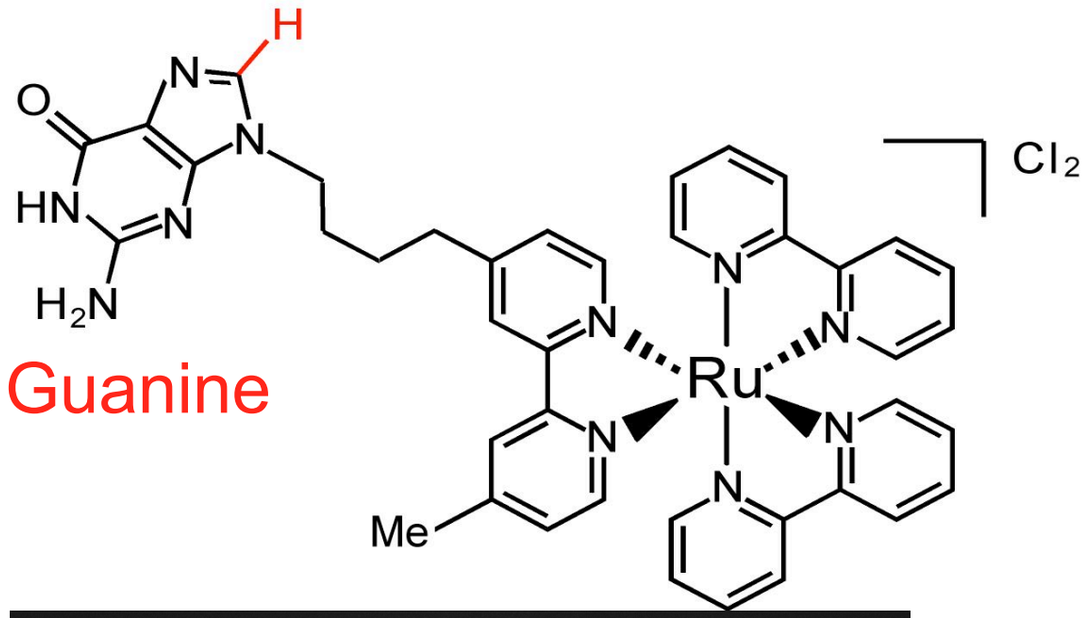
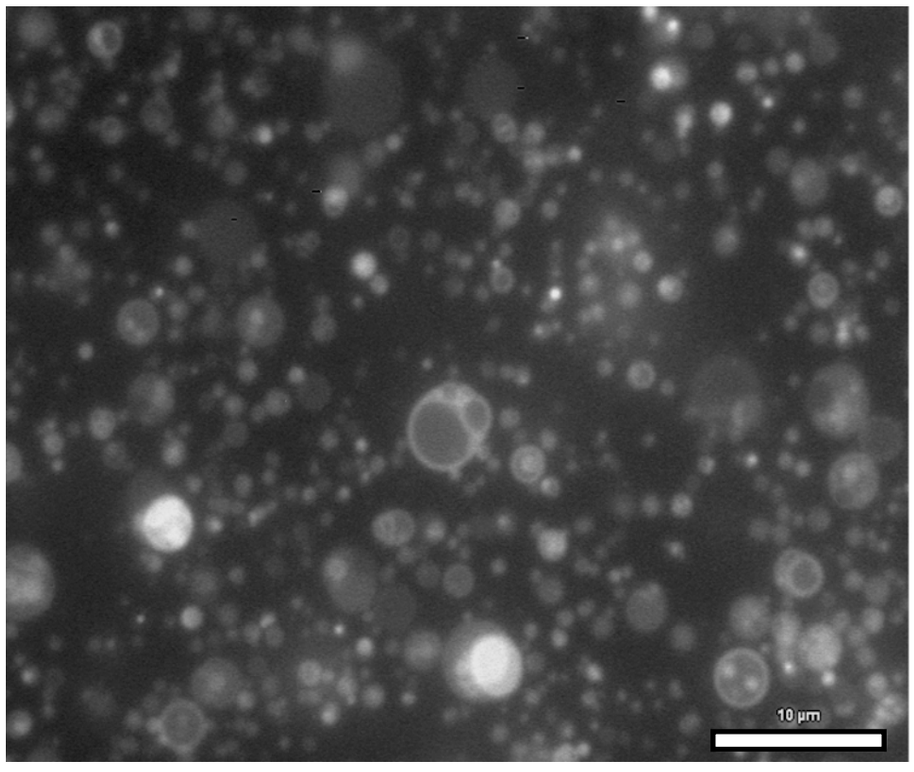


Guanine



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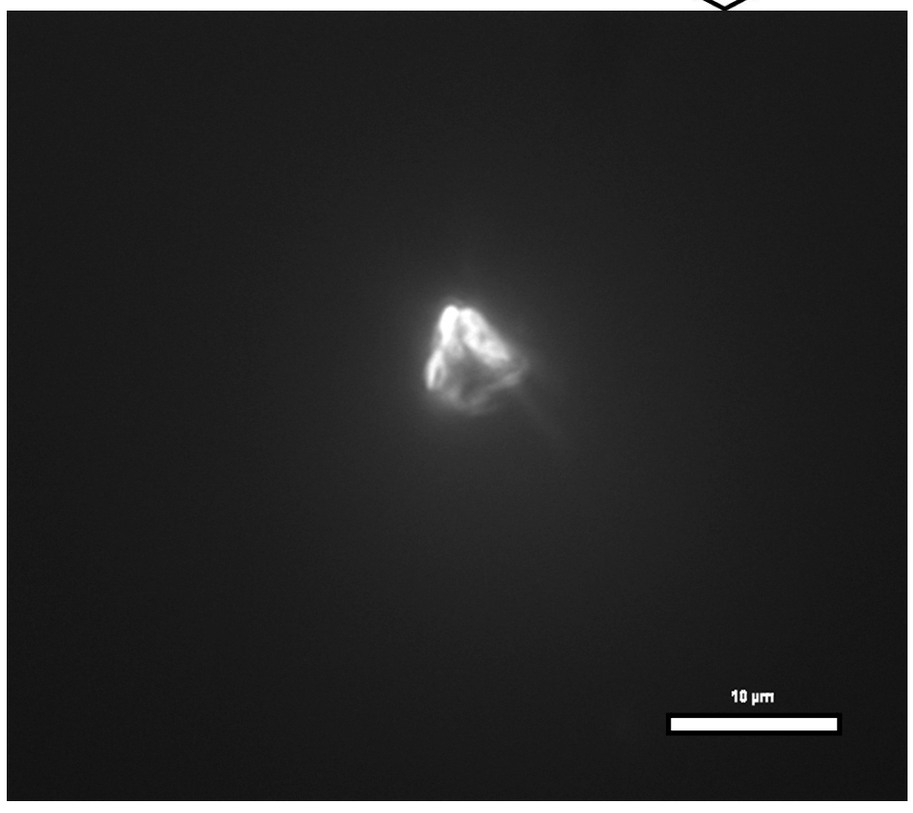


Oil and crystals only (<10%)

Declue et al 2009 JACS

Influence of the reaction set-up on precursor conversion (initial rates)

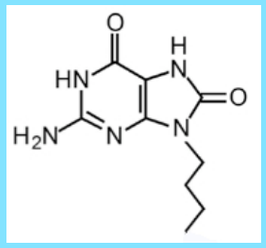
Reaction: 0.1 mM catalyst, 5 mM of precursor, 15.75 mM H-source. With vesicles: 10 mM Decanoic acid

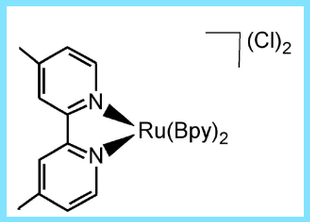
Maurer et al 2011 ChemPhysChem

Influence of the reaction set-up on precursor conversion (initial rates)

Intermolecular

aqueous





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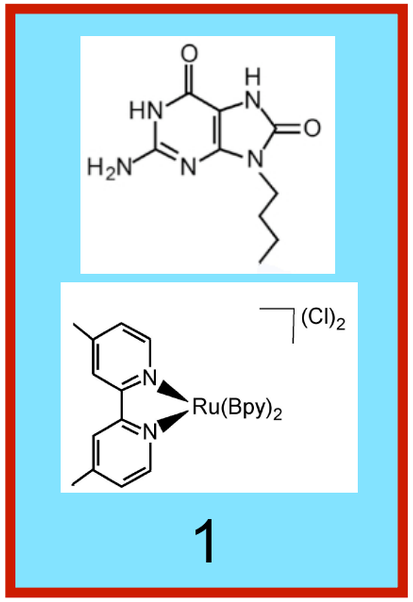
Reaction: 0.1 mM catalyst, 5 mM of precursor, 15.75 mM H-source. With vesicles: 10 mM Decanoic acid

Influence of the reaction set-up on precursor conversion (initial rates)

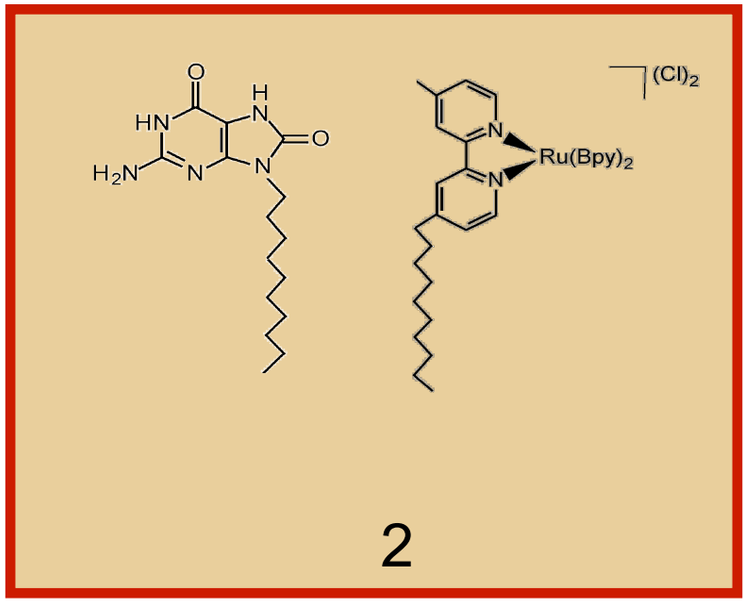
Intermolecular

aqueous

oil/bilayer linked



1



2

Reaction: 0.1 mM catalyst, 5 mM of precursor, 15.75 mM H-source. With vesicles: 10 mM Decanoic acid

Maurer et al 2011 ChemPhysChem

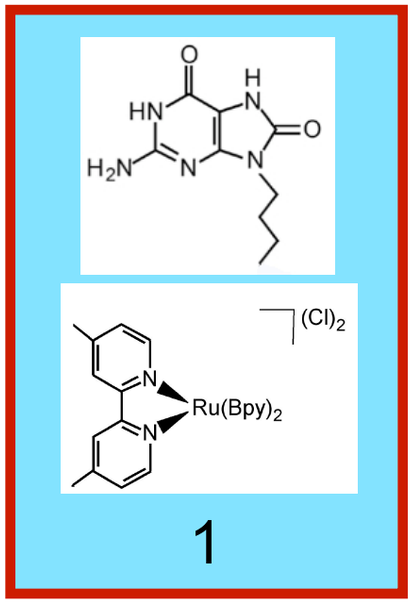
Influence of the reaction set-up on precursor conversion (initial rates)

Intermolecular

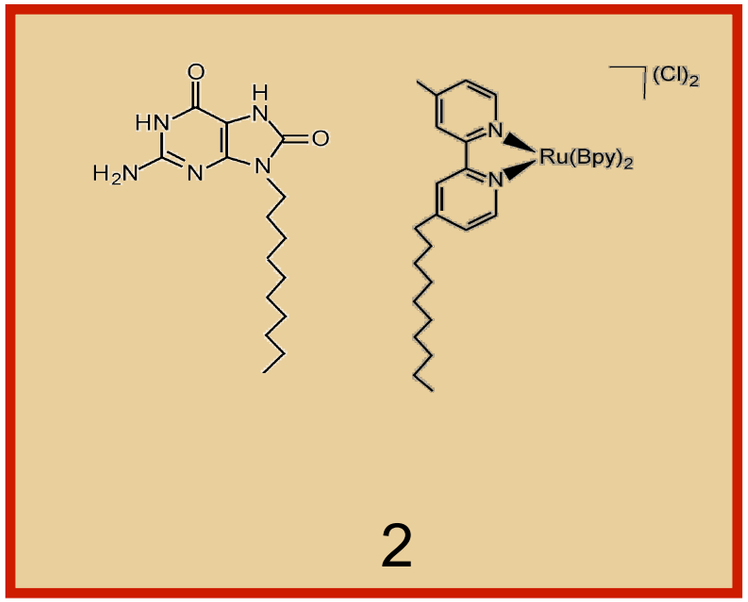
intramolecular

aqueous

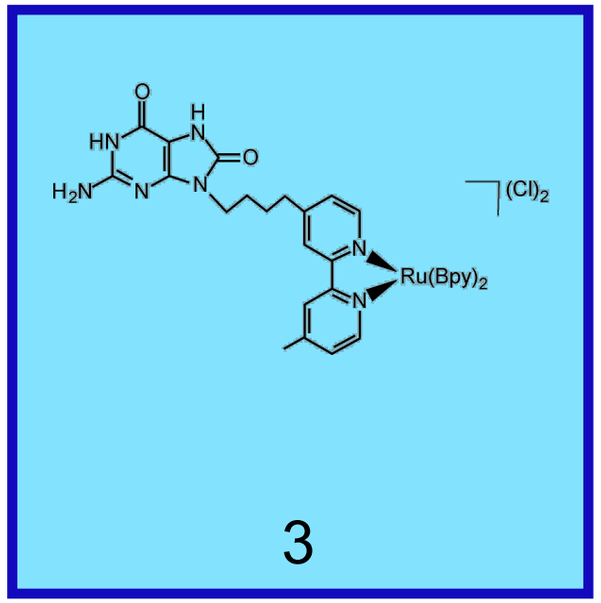
oil/bilayer linked



1



2

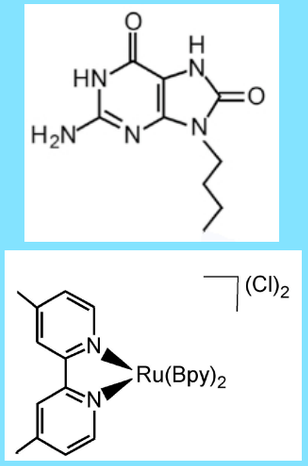


3

Reaction: 0.1 mM catalyst, 5 mM of precursor, 15.75 mM H-source. With vesicles: 10 mM Decanoic acid

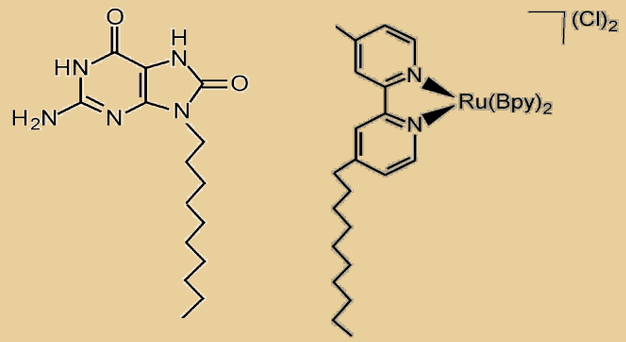
Influence of the reaction set-up on precursor conversion (initial rates)

Intermolecular



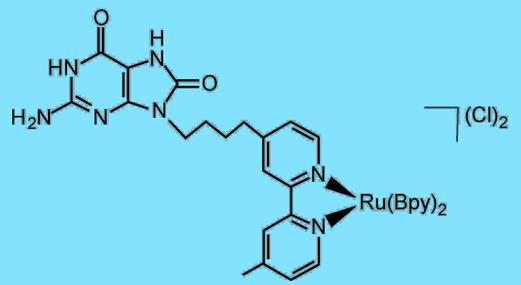
1

intramolecular



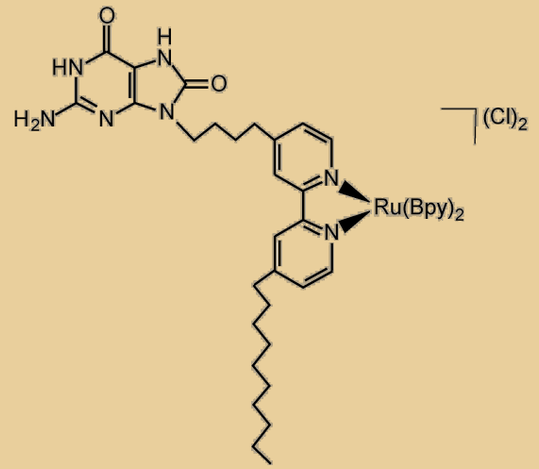
2

aqueous



3

oil/bilayer linked

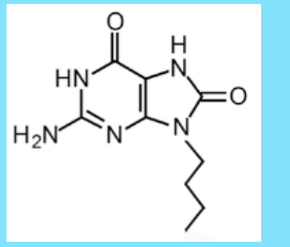


4

Reaction: 0.1 mM catalyst, 5 mM of precursor, 15.75 mM H-source. With vesicles: 10 mM Decanoic acid

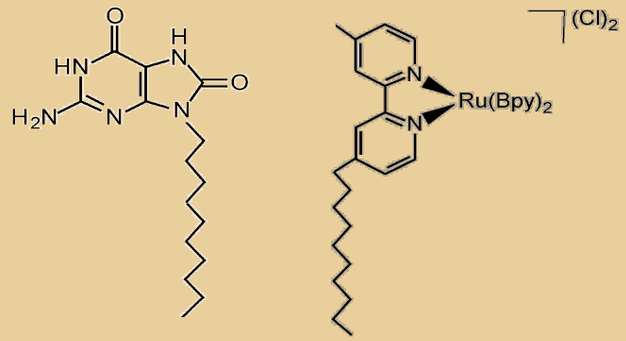
Influence of the reaction set-up on precursor conversion (initial rates)

Intermolecular



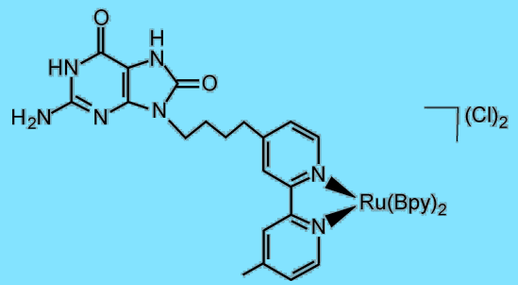
1

intramolecular



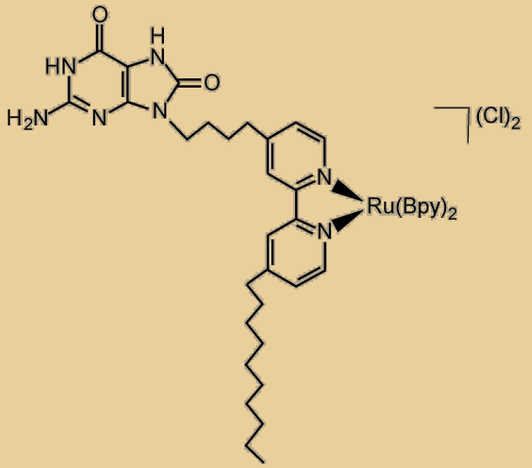
2

aqueous



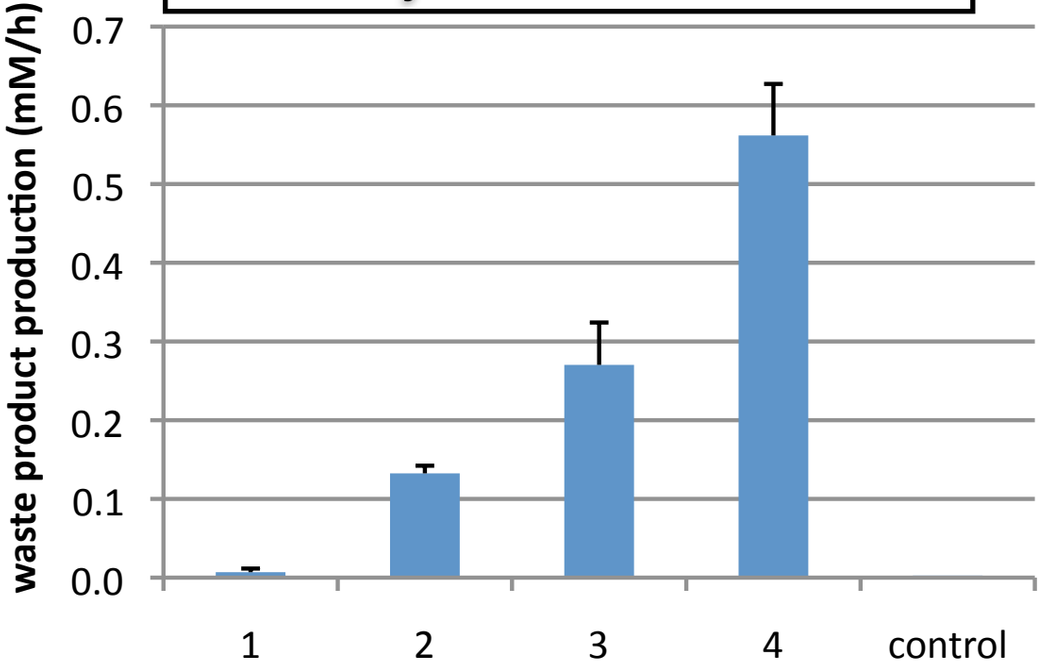
3

oil/bilayer linked



4

no bilayers = no container



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Maurer et al 2011 ChemPhysChem

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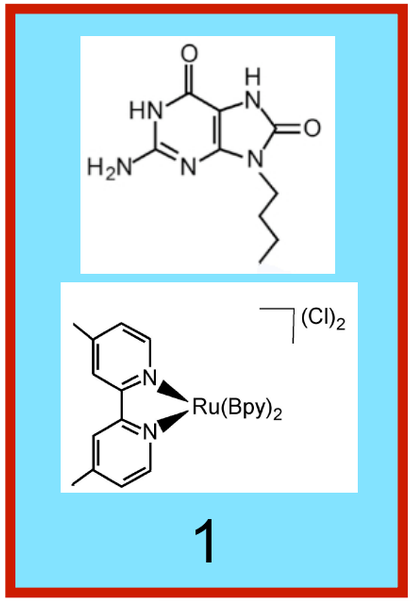
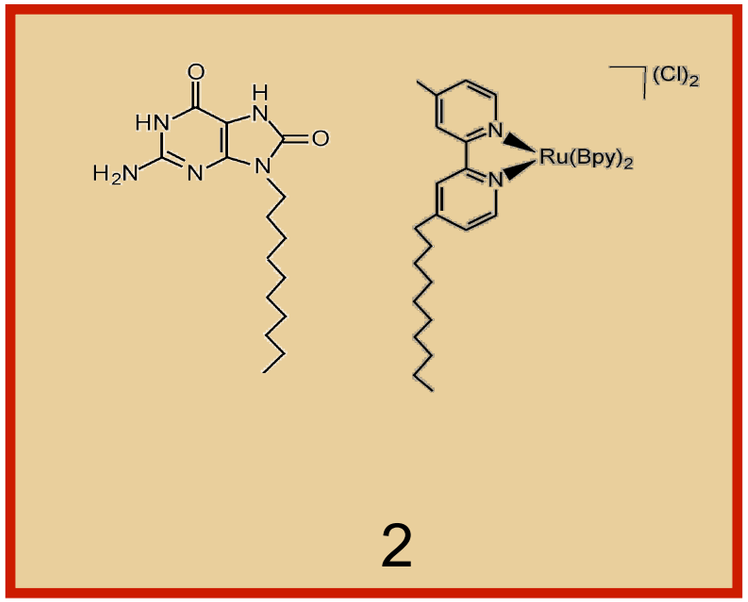
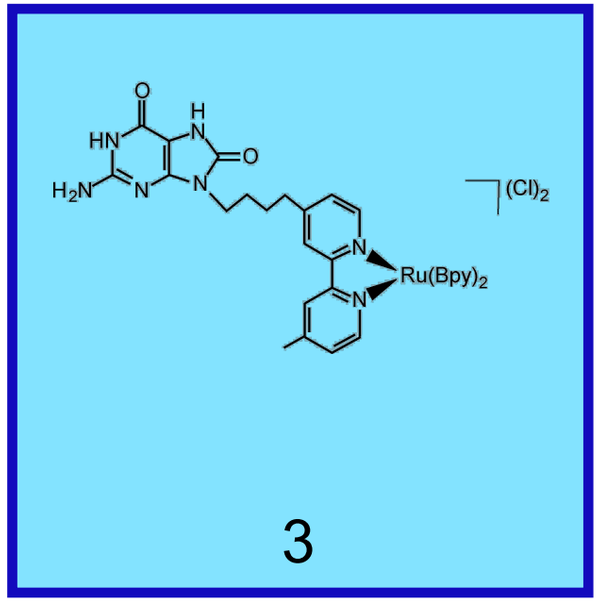
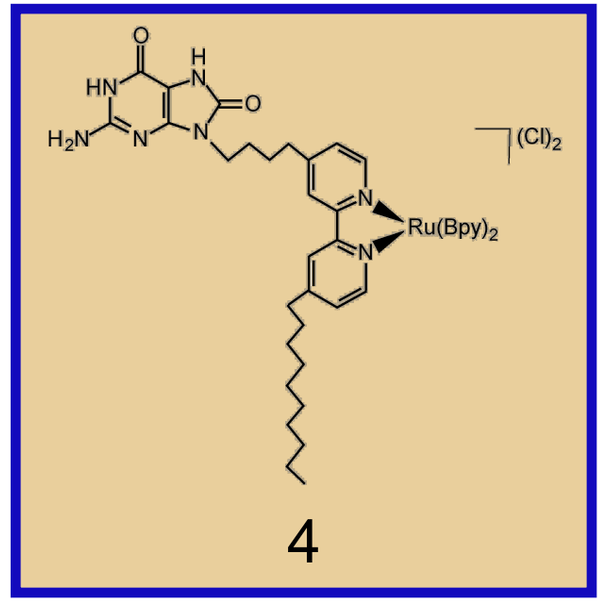
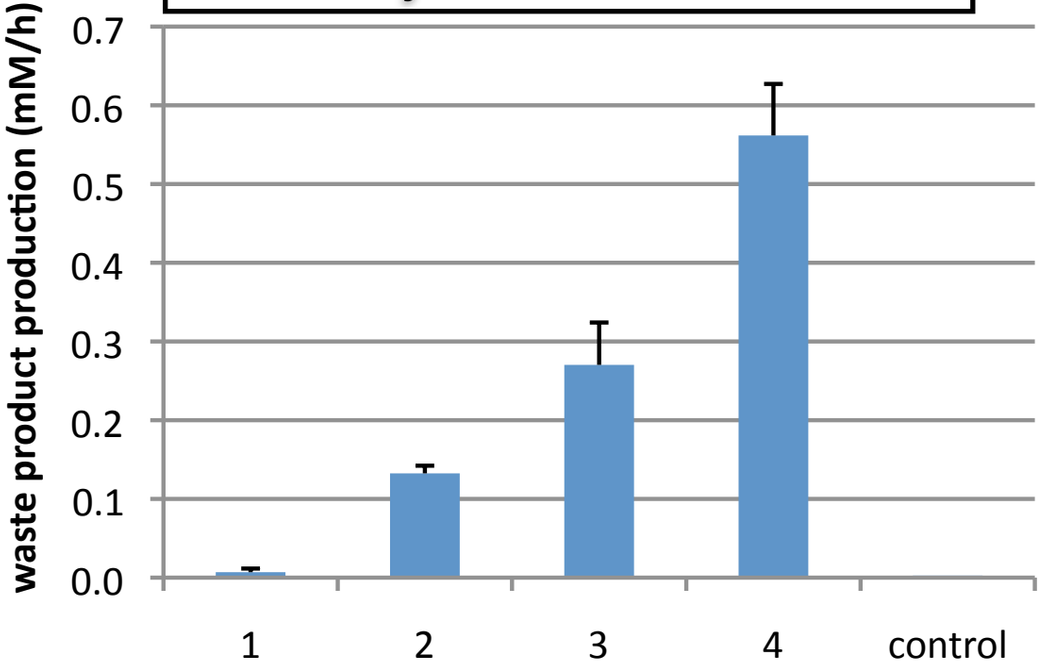




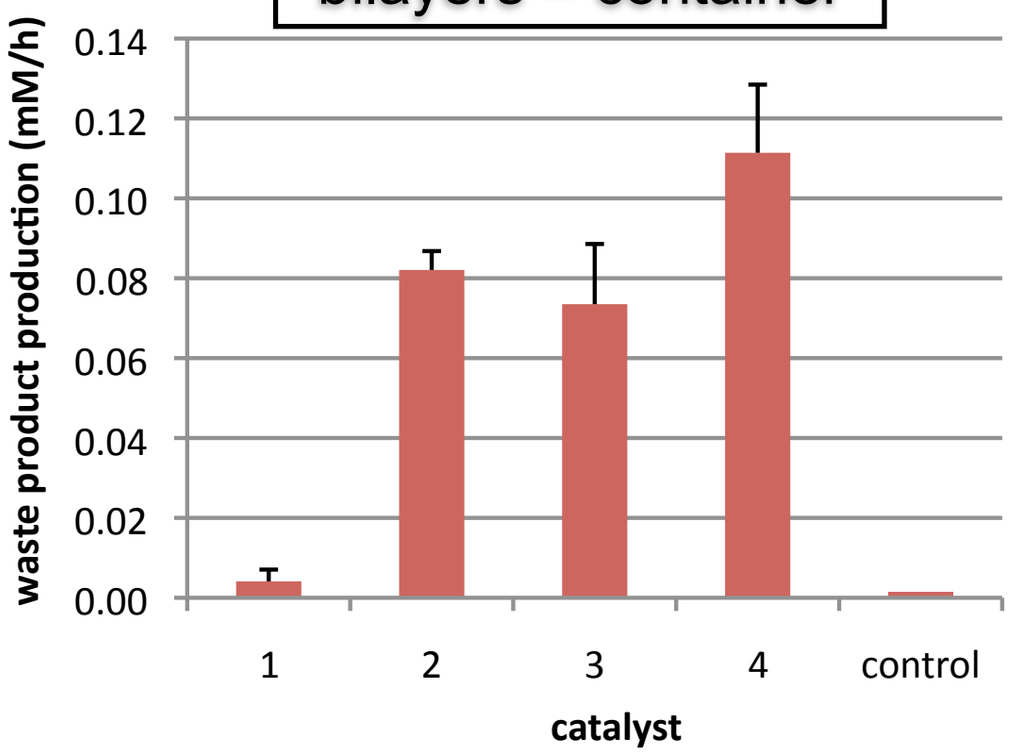




no bilayers = no container



bilayers = container



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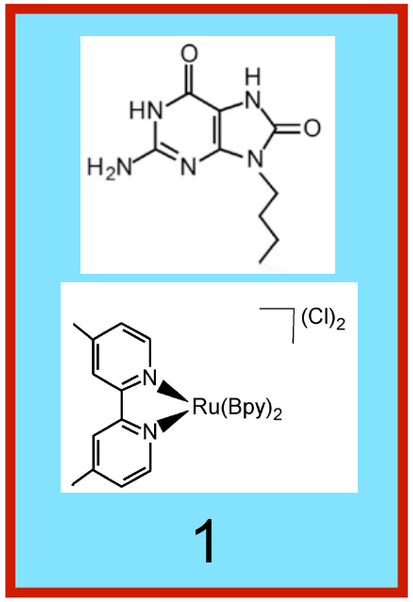
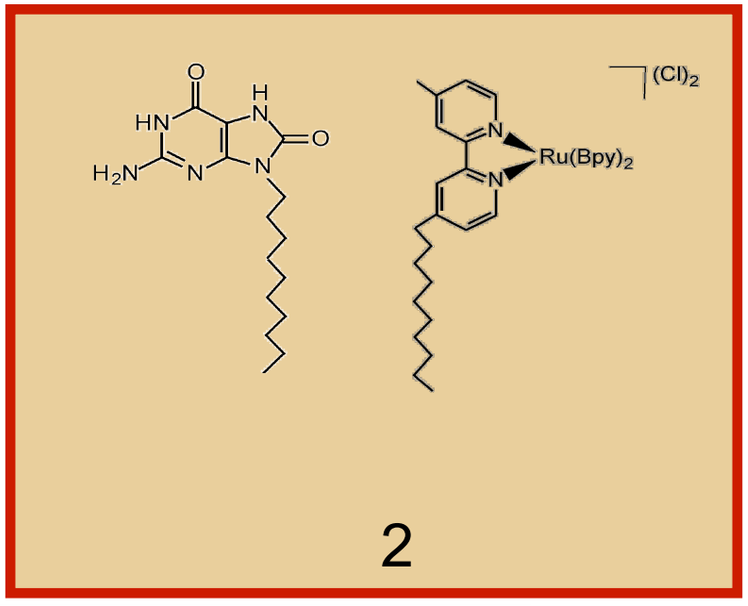
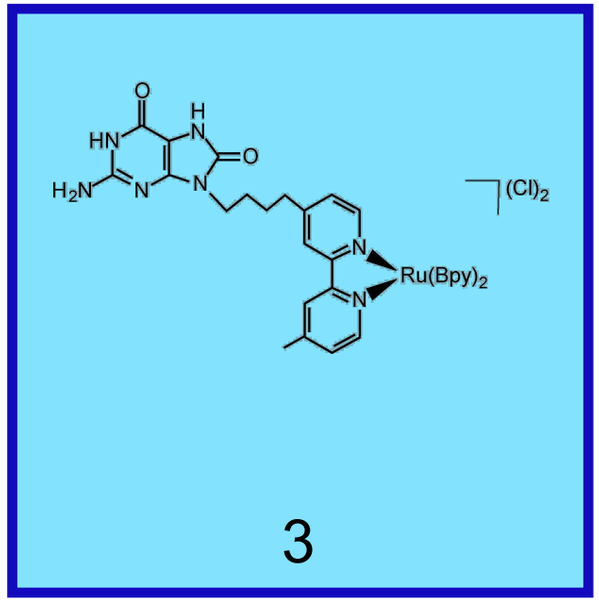
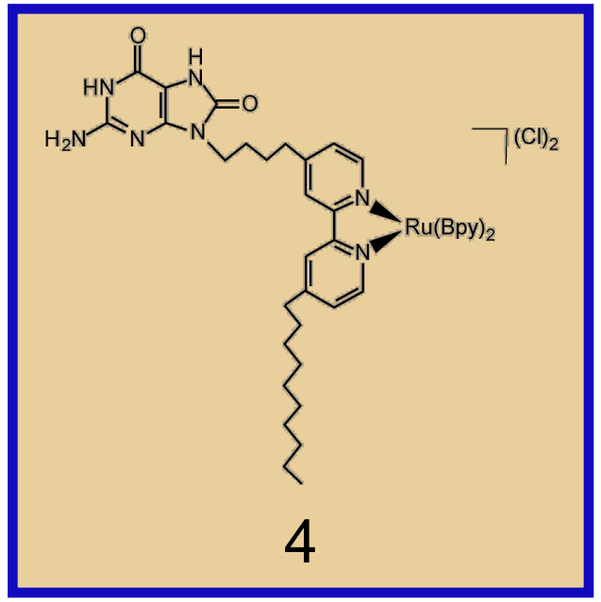
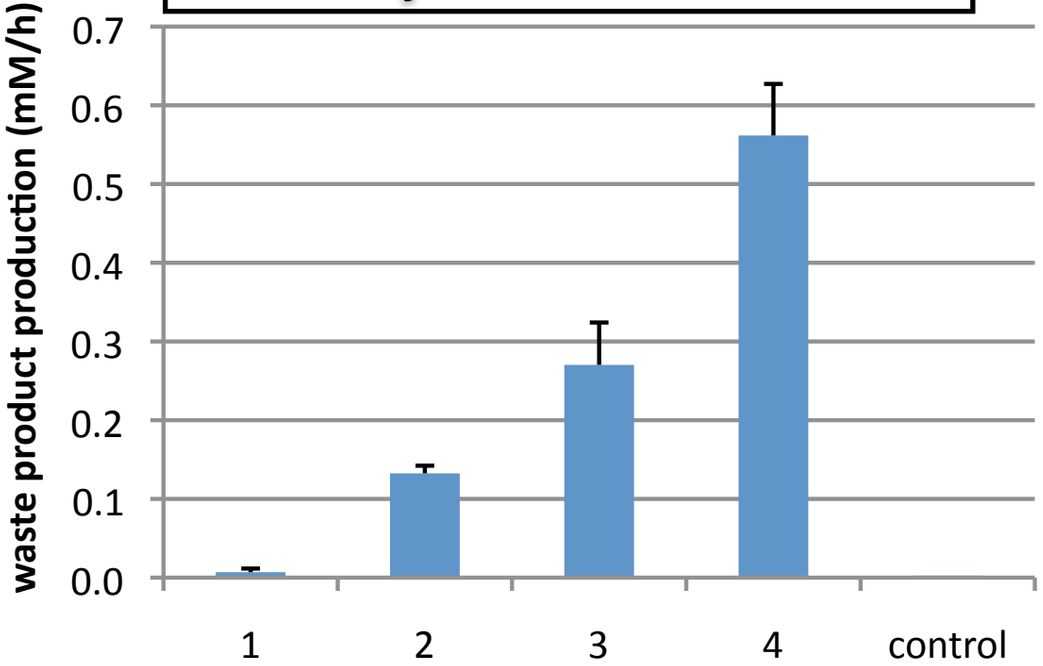




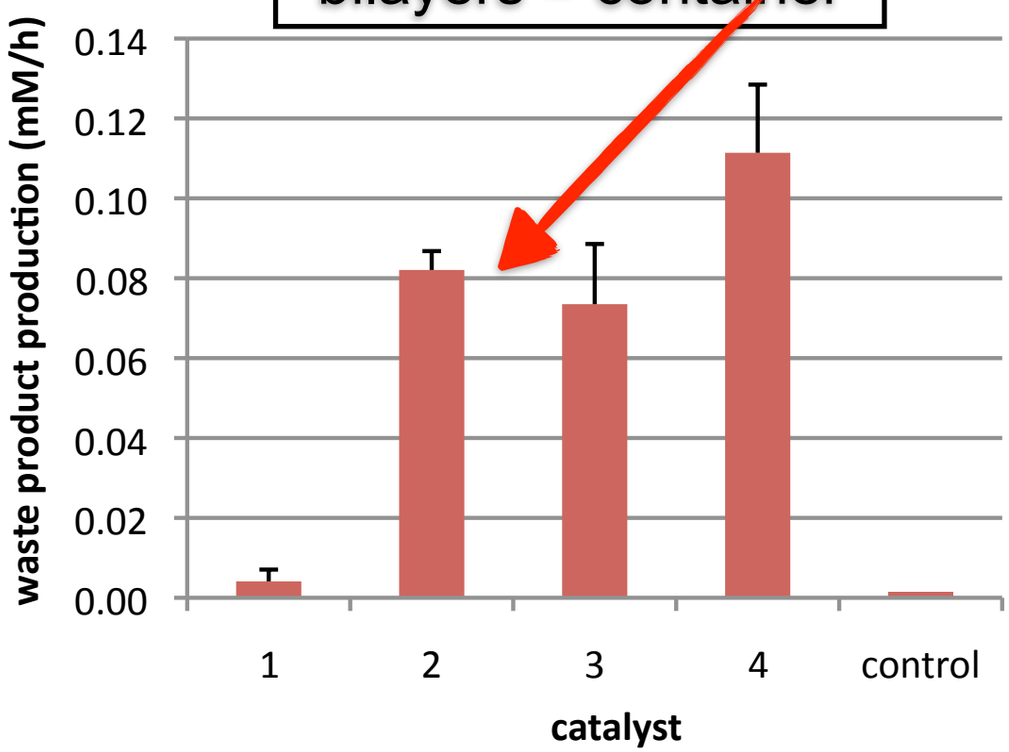




no bilayers = no container

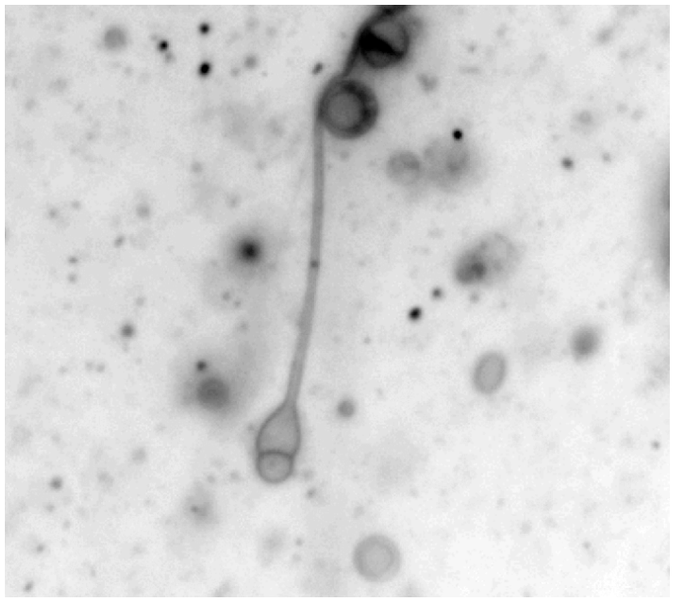


bilayers = container



Reaction: 0.1 mM catalyst, 5 mM of precursor, 15.75 mM H-source. With vesicles: 10 mM Decanoic acid

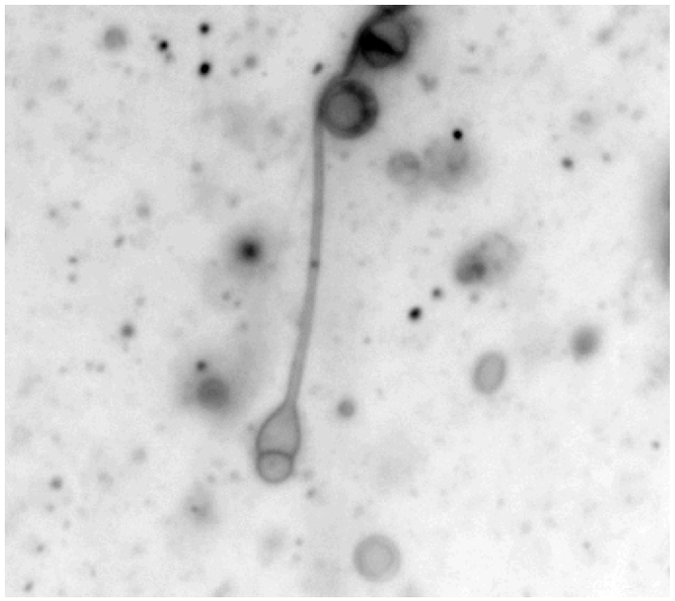
Observation of a complete life cycle



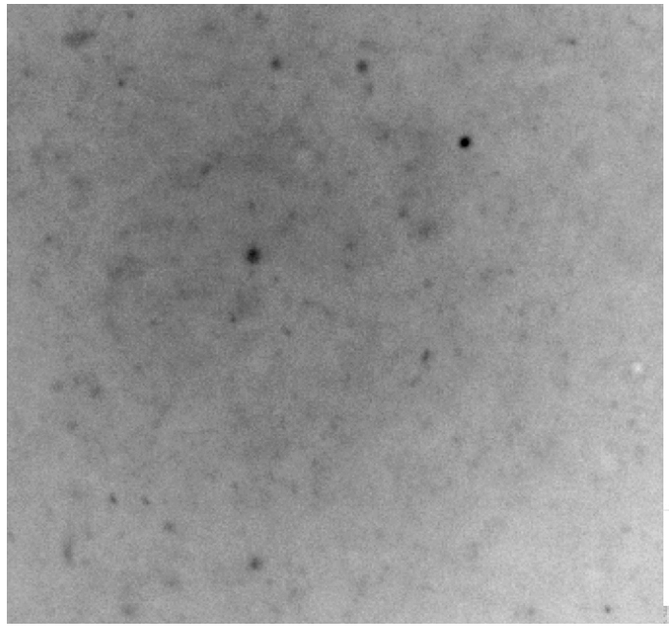
bar = 25 µm

Maurer & Albertsen

Observation of a complete life cycle



Homogenization



bar = 25 µm

Maurer & Albertsen

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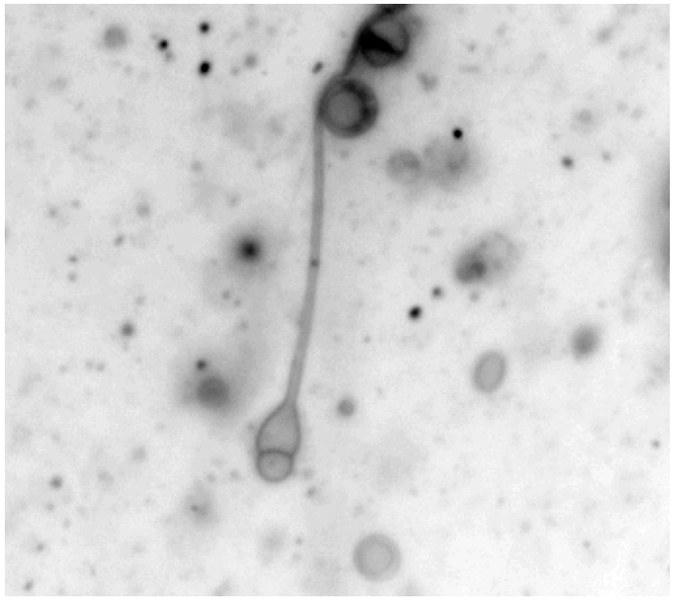
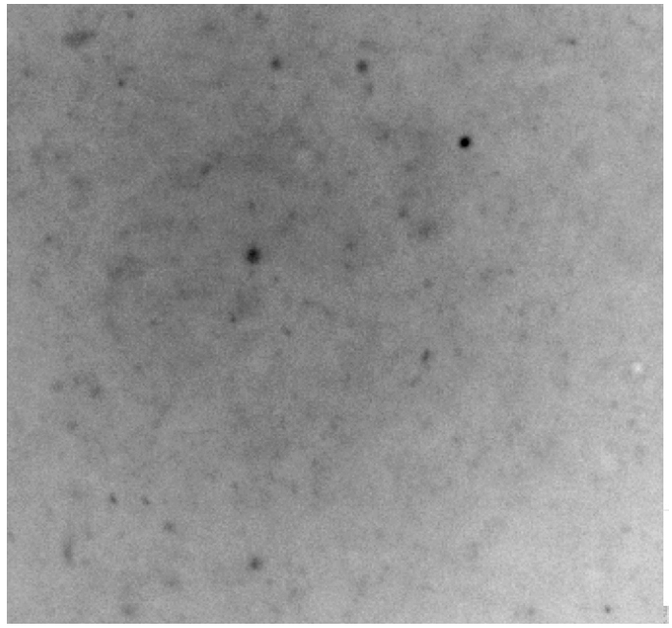
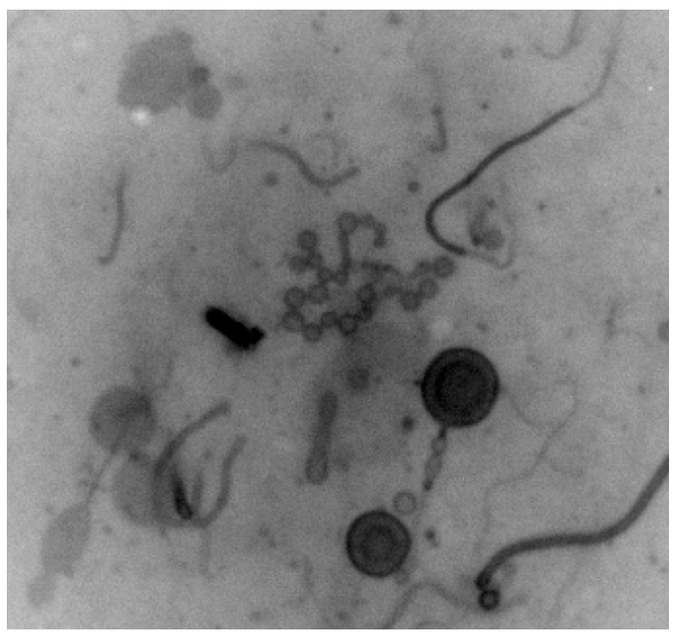


Homogenization



Nutrient uptake



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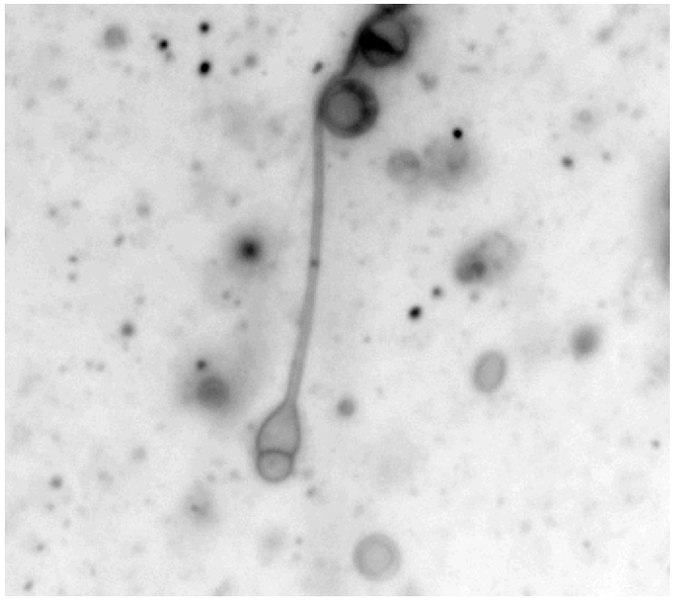
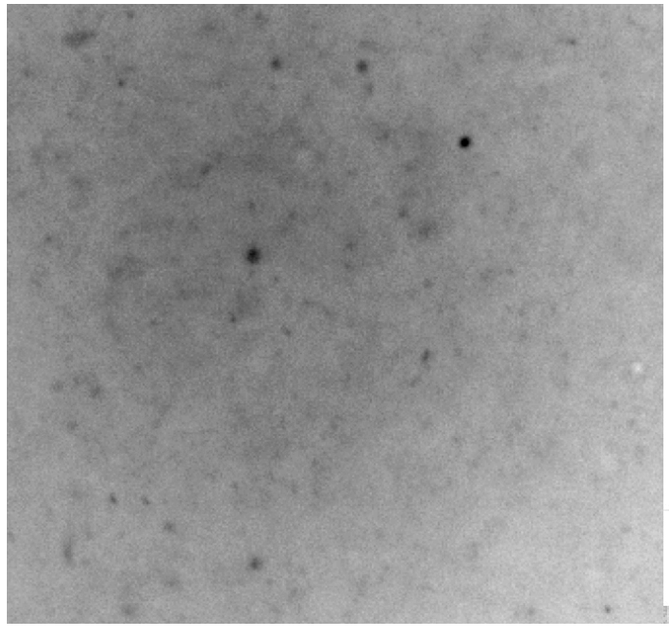
Maurer & Albertsen

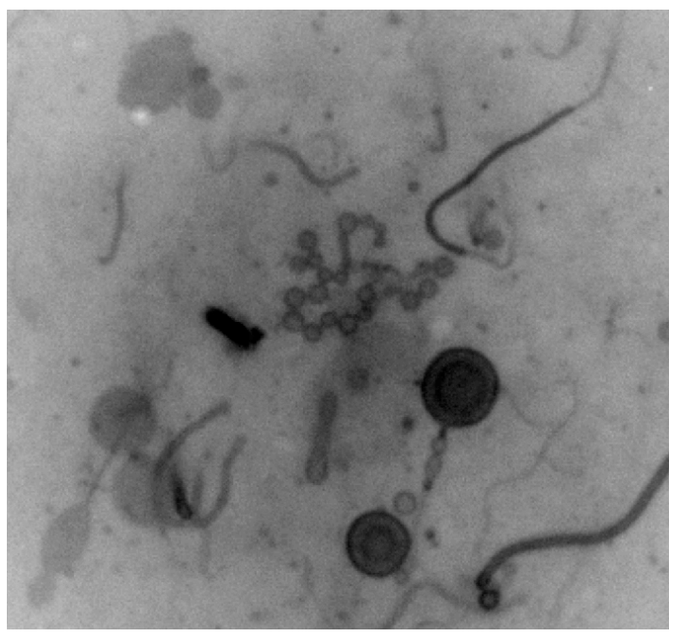
Observation of a complete life cycle



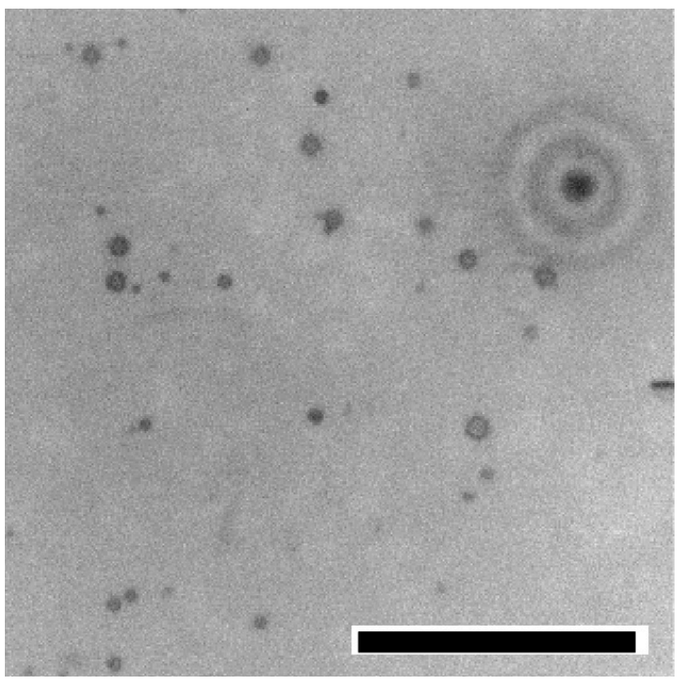
Homogenization



Nutrient uptake



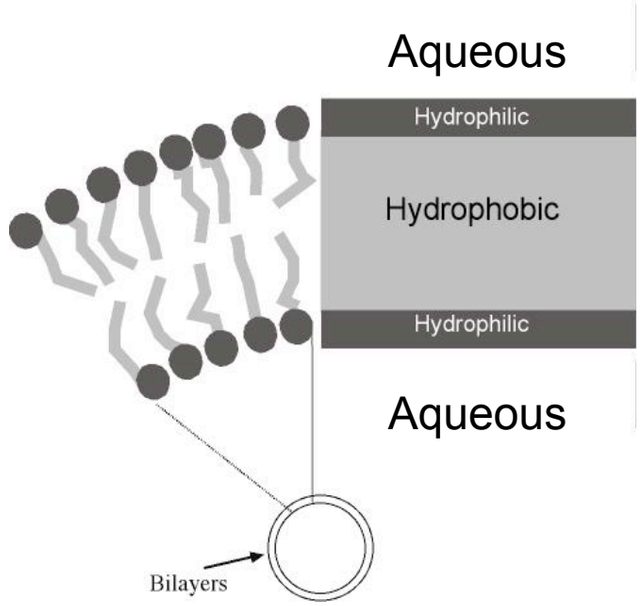
Metabolic amphiphile production



bar = 25 µm

Maurer & Albertsen

Other possible functions of primitive membranes: Can primitive membranes promote reactions?



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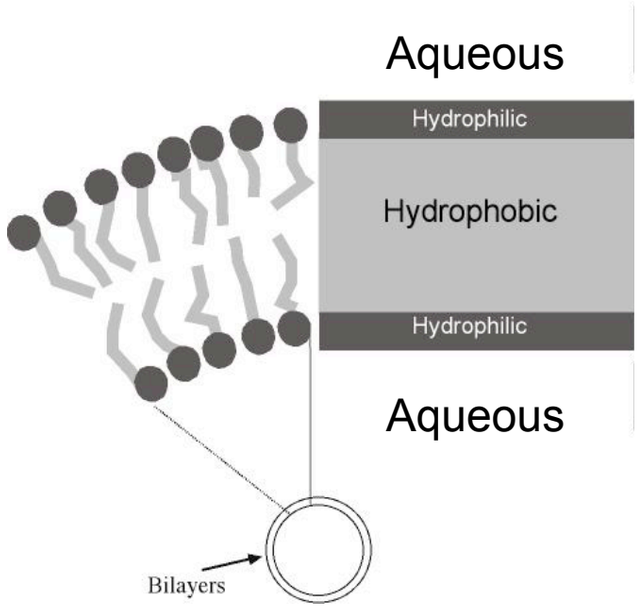
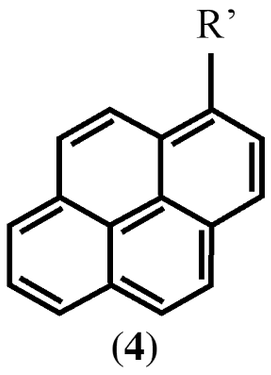
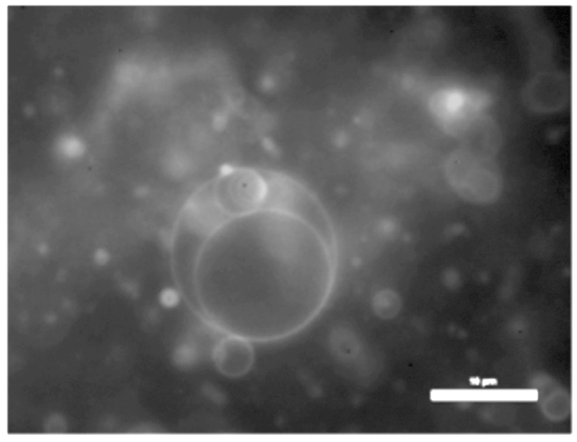
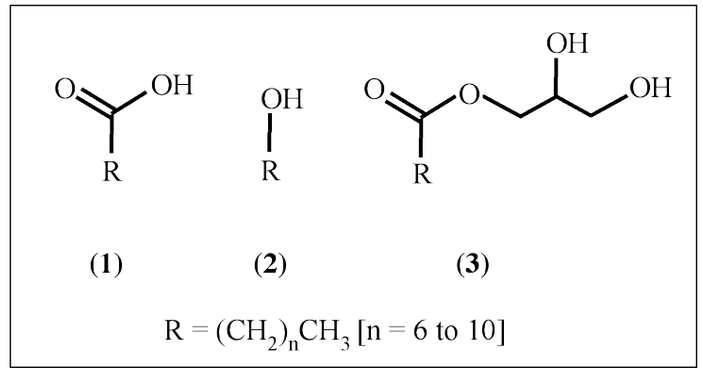


Chemical autonomy by internalized production of chemicals using light harvesting systems

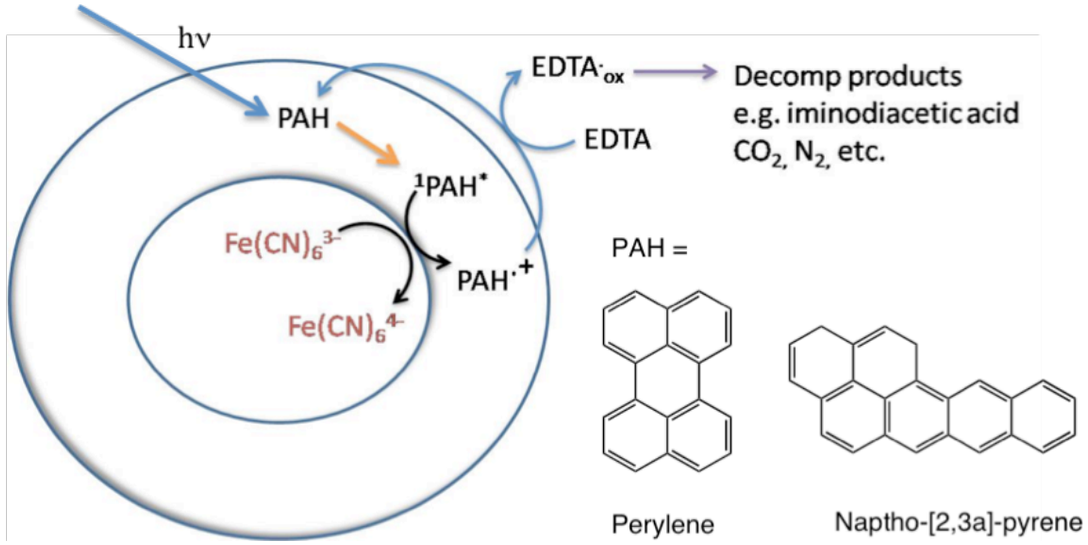


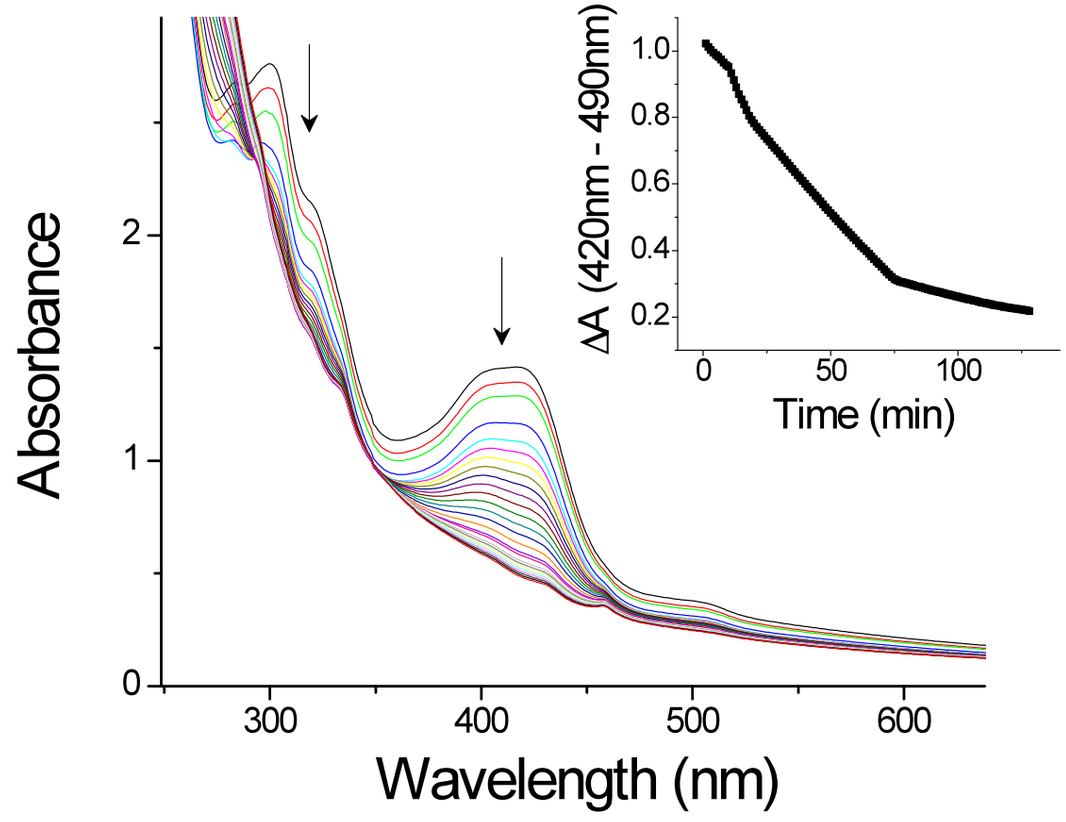
(4) Pyrene and its derivatives





Fatty (1) acids, (2) alcohols, (3) monoacyl-glycerol. Epifluorescence micrographs from suspensions of decanoic acid (1) with n equals 9. Bars = 10 µm.





Cape et al., 2011 Chem Sci

Other Quasi-compartmentalization
self-replication of early genetic/catalytic material

Lipid matrices: Principle

Courtesy of D. W. Deamer

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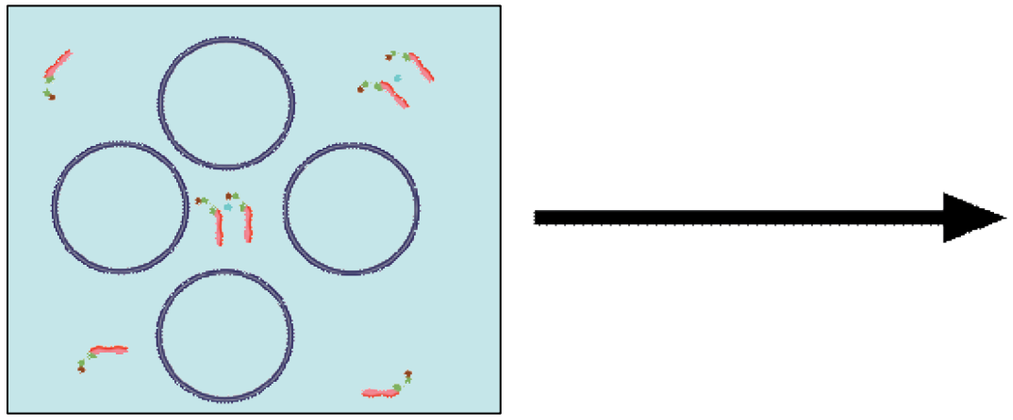
self-replication of early genetic/catalytic material

Lipid matrices: Principle



Aqueous suspension

Courtesy of D. W. Deamer

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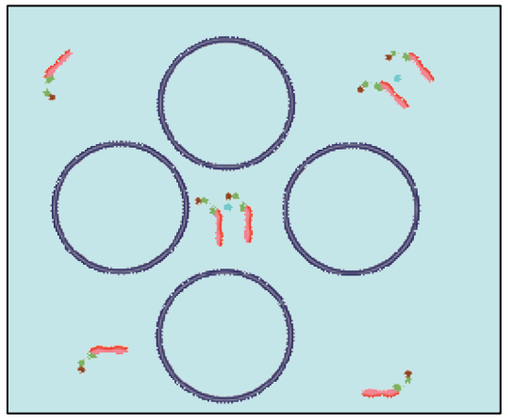
self-replication of early genetic/catalytic material

Lipid matrices: Principle



Dehydration

Aqueous suspension

Courtesy of D. W. Deamer

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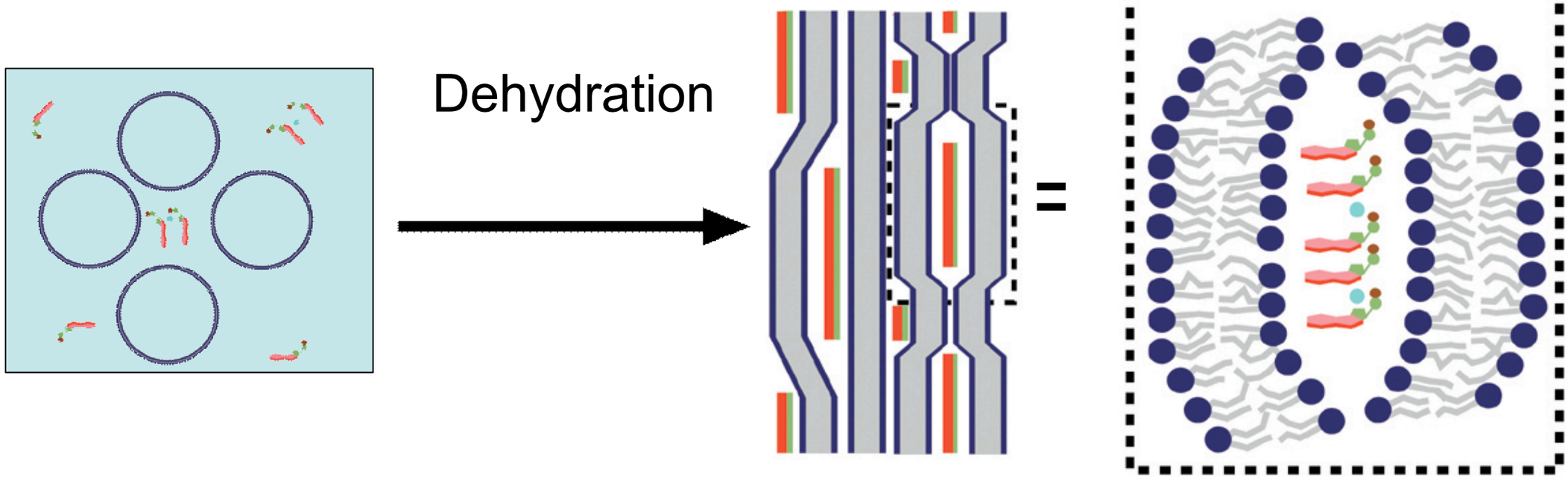
Lipid matrices: Principle



Aqueous suspension Dried film Liquid crystalline lipid phase

Courtesy of D. W. Deamer

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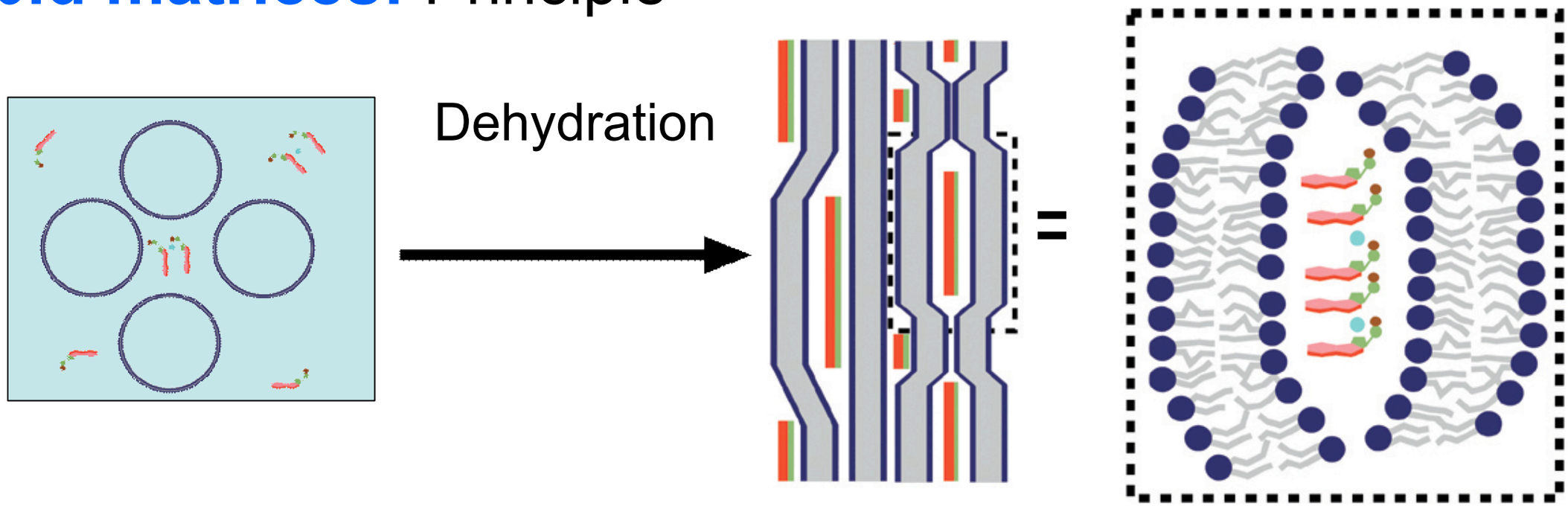
Lipid matrices: Principle

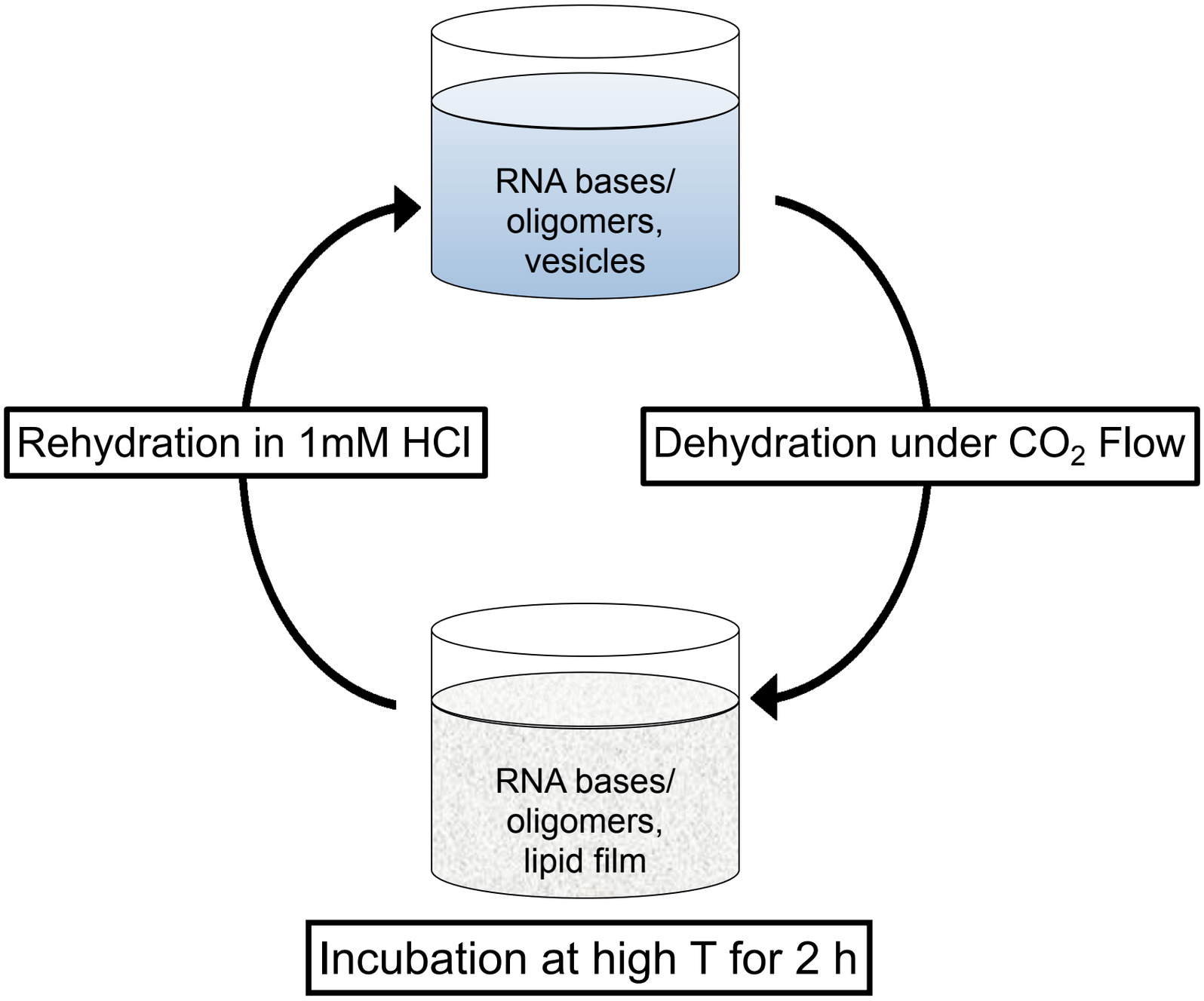


Aqueous suspension Dried film Liquid crystalline lipid phase

DOPC/DNA (2:1)
ffEM: Pt,C shadowing

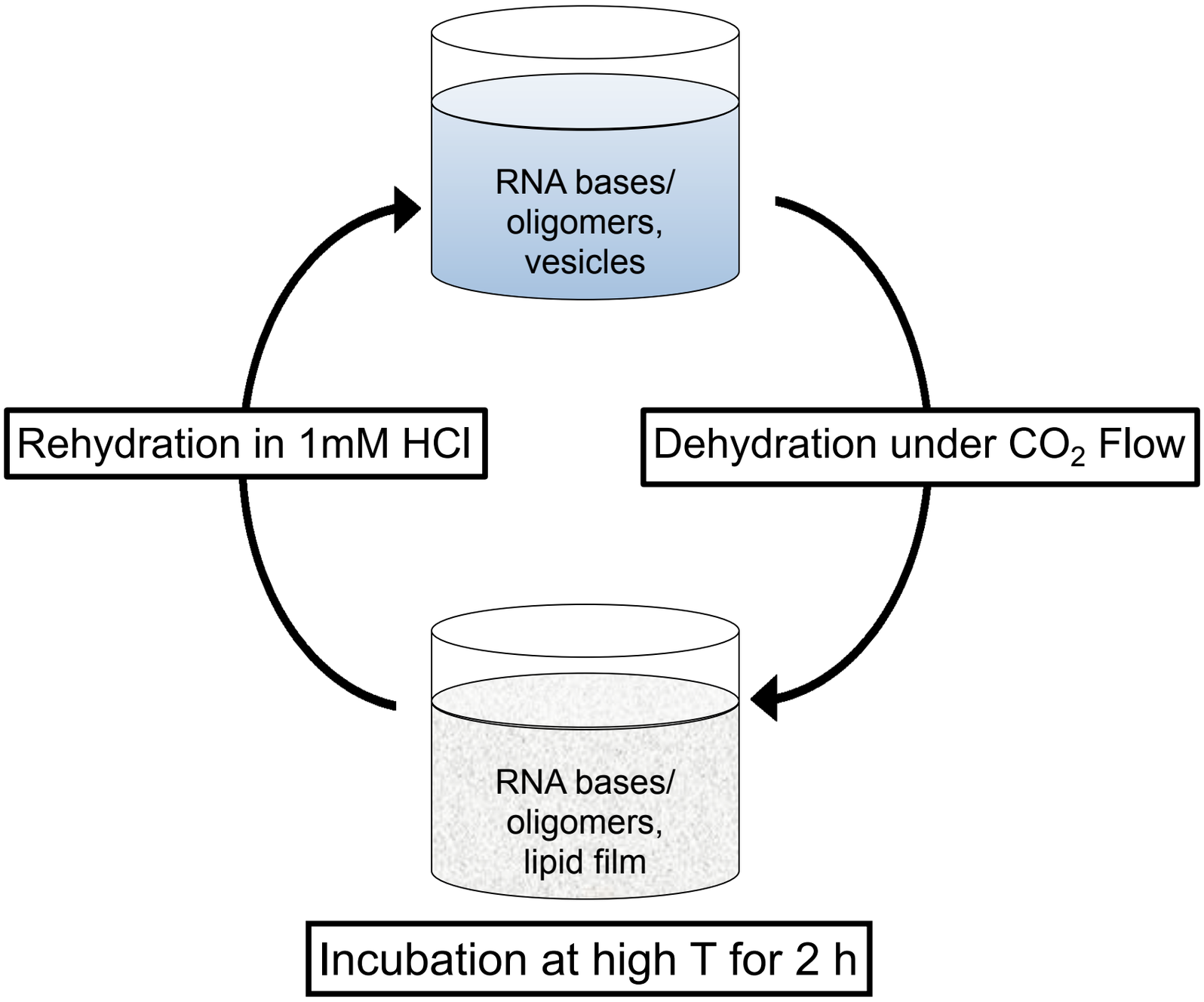
Courtesy of D. W. Deamer

Dehydration-Rehydration cycles: Non-enzymatic RNA polymerization

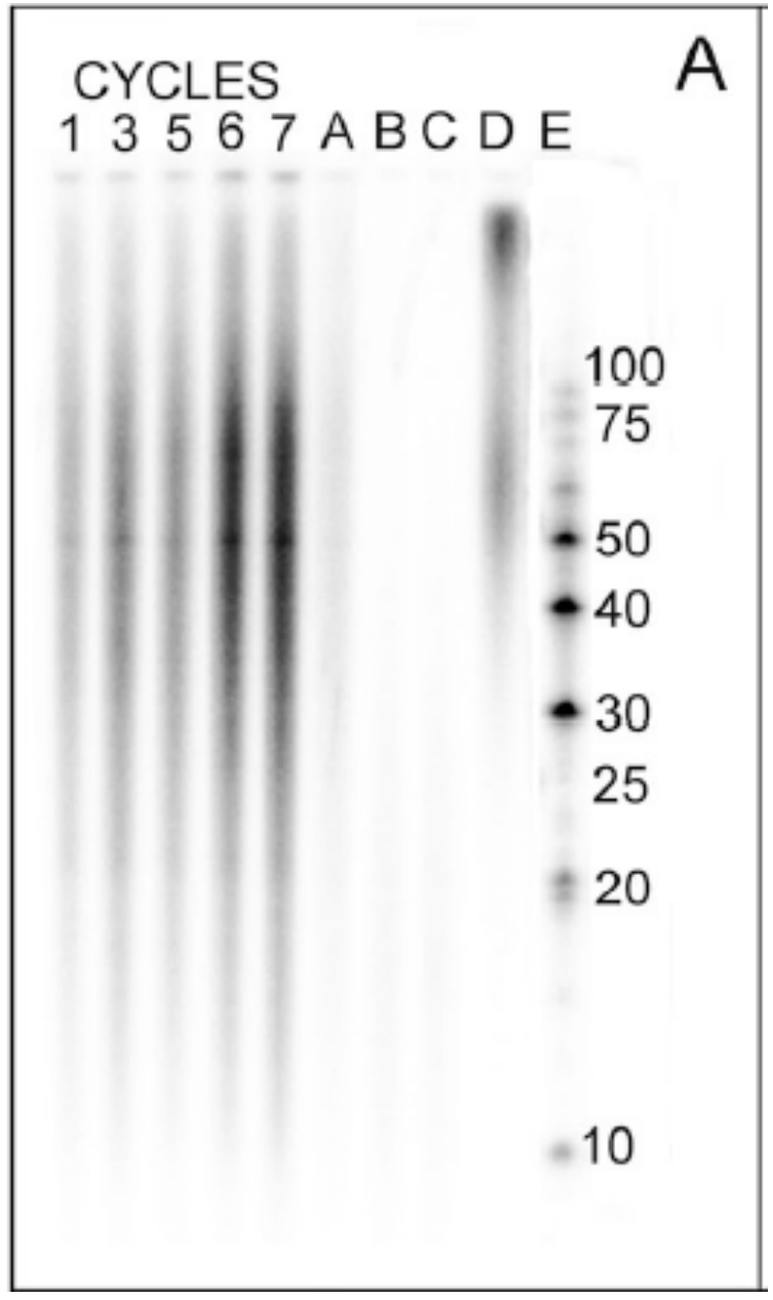


Rajamani, S., et al. Orig Life Evol Biosph (2008) 38:57-74

Dehydration-Rehydration cycles: Non-enzymatic RNA polymerization

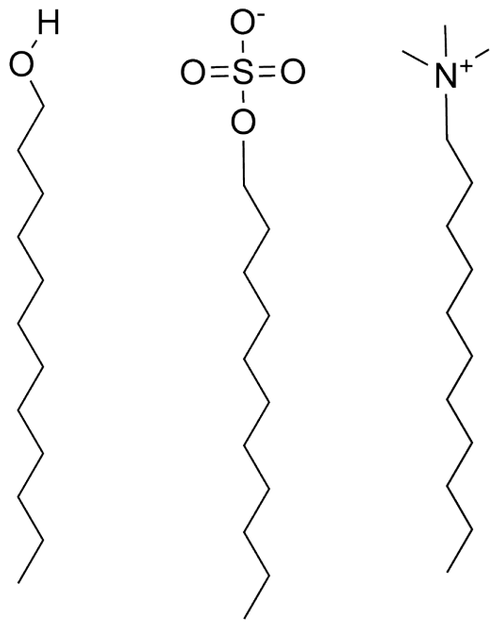


Phosphatidyl lipids and lysolipids



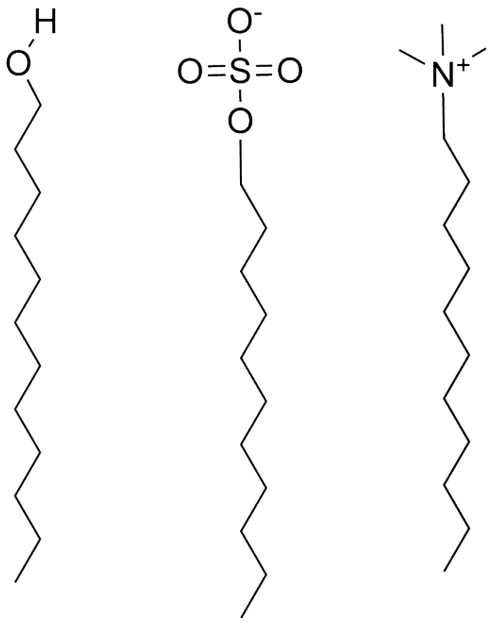
Rajamani, S., et al. Orig Life Evol Biosph (2008) 38:57-74

Morphology of hydrated/dried “prebiotic” samples



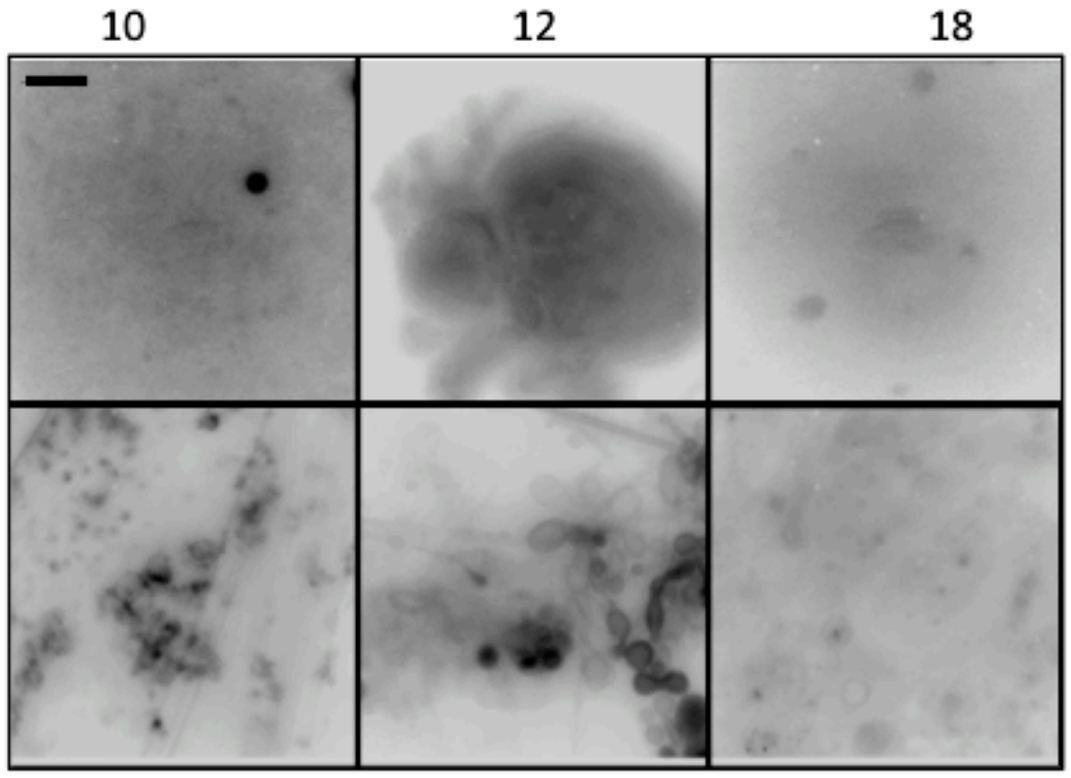
bar = 10 µm

Morphology of hydrated/dried “prebiotic” samples



Alkyl alcohols

Alkyl trimethyl ammoniums



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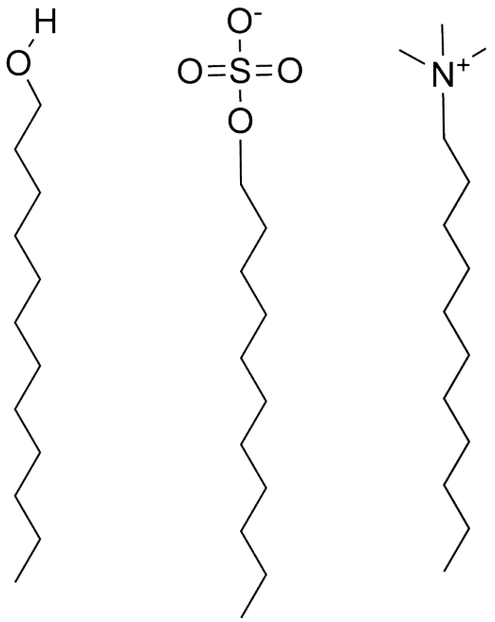
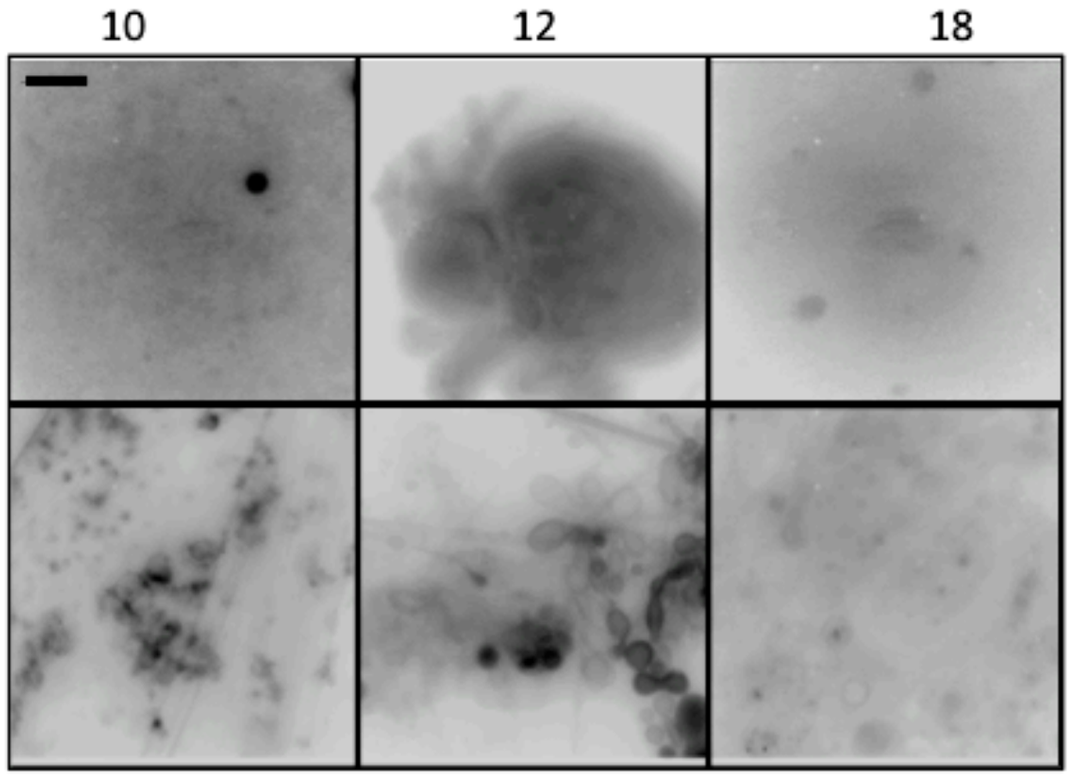


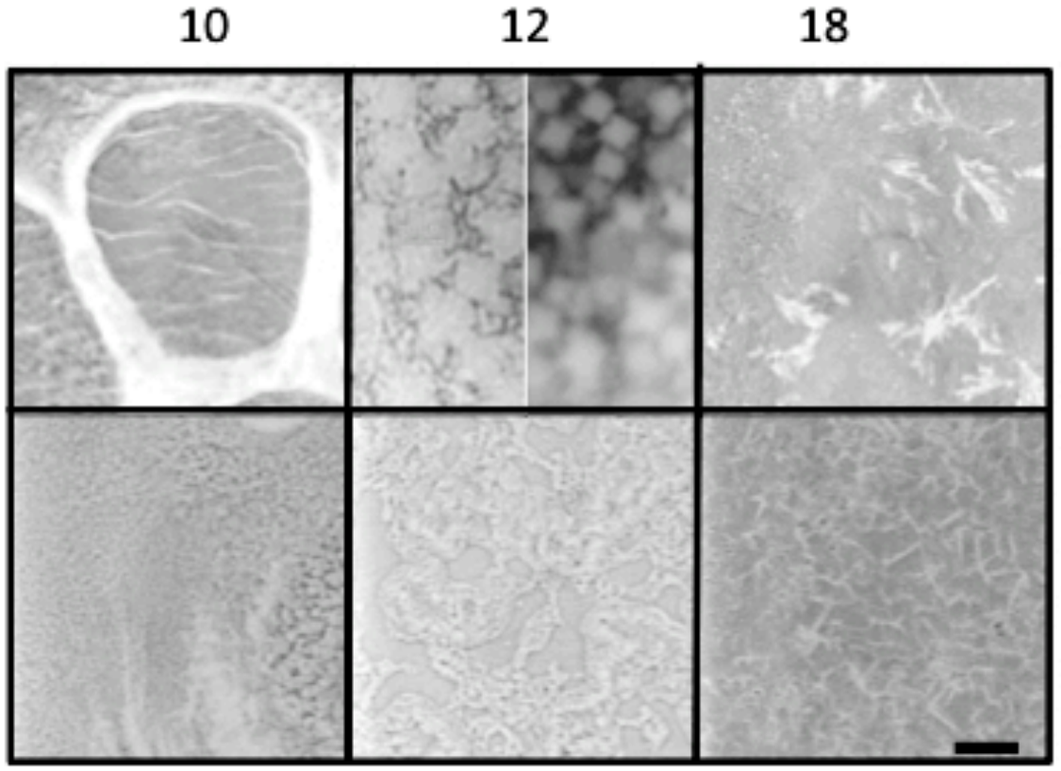
Alkyl alcohols

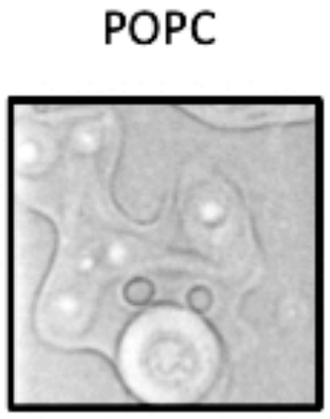
Alkyl trimethyl ammoniums



Alkyl alcohols

Alkyl trimethyl ammoniums

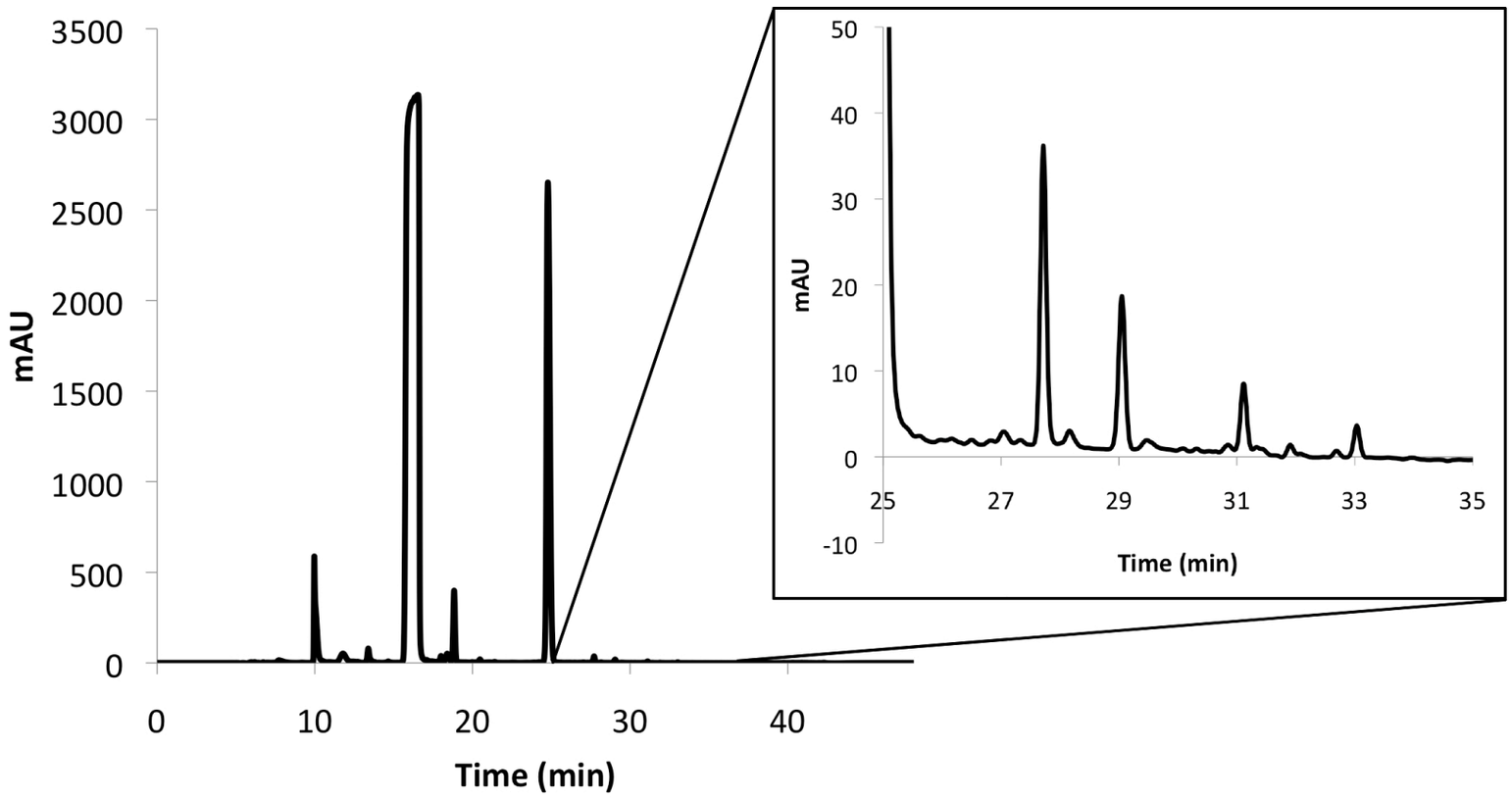




bar = 10 μm

Shorter product analysis

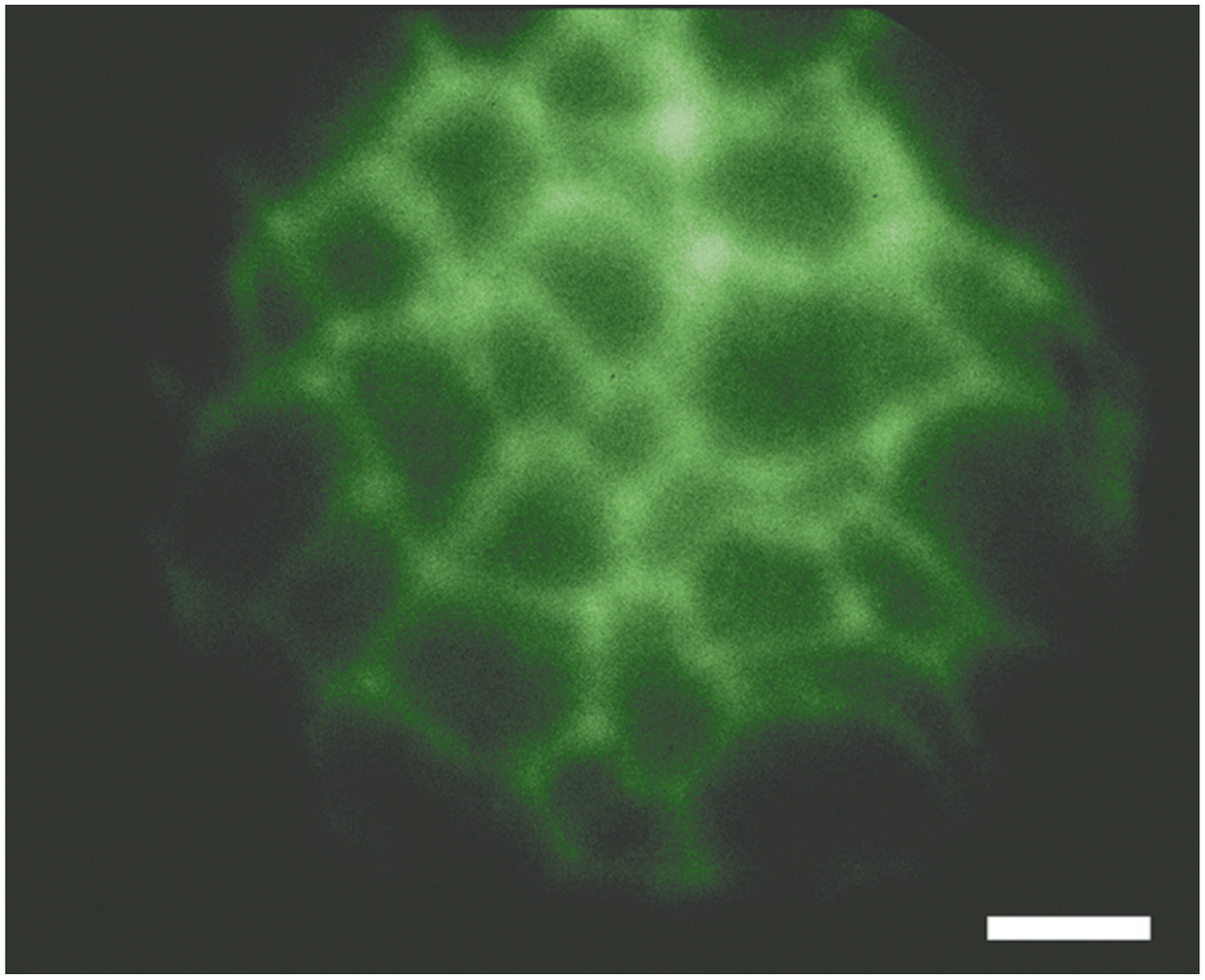
AMP + amphiphiles (mol ratio 1:2)



After reaction cycle 8 all samples showed formation of a product at 25 min. by RP HPLC

Maurer 2010

Quasi-compartmentalization in EUTECTIC PHASE IN WATER-ICE

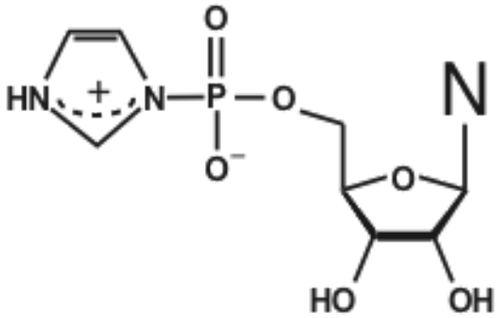


Upon the initiation of freezing, the concentration of the solutes increases which simultaneously lowers the freezing point of the residual solution.

Epifluorescence micrograph of monomer suspension used in self-condensation experiments. Acridine Orange was added to visualize the structures

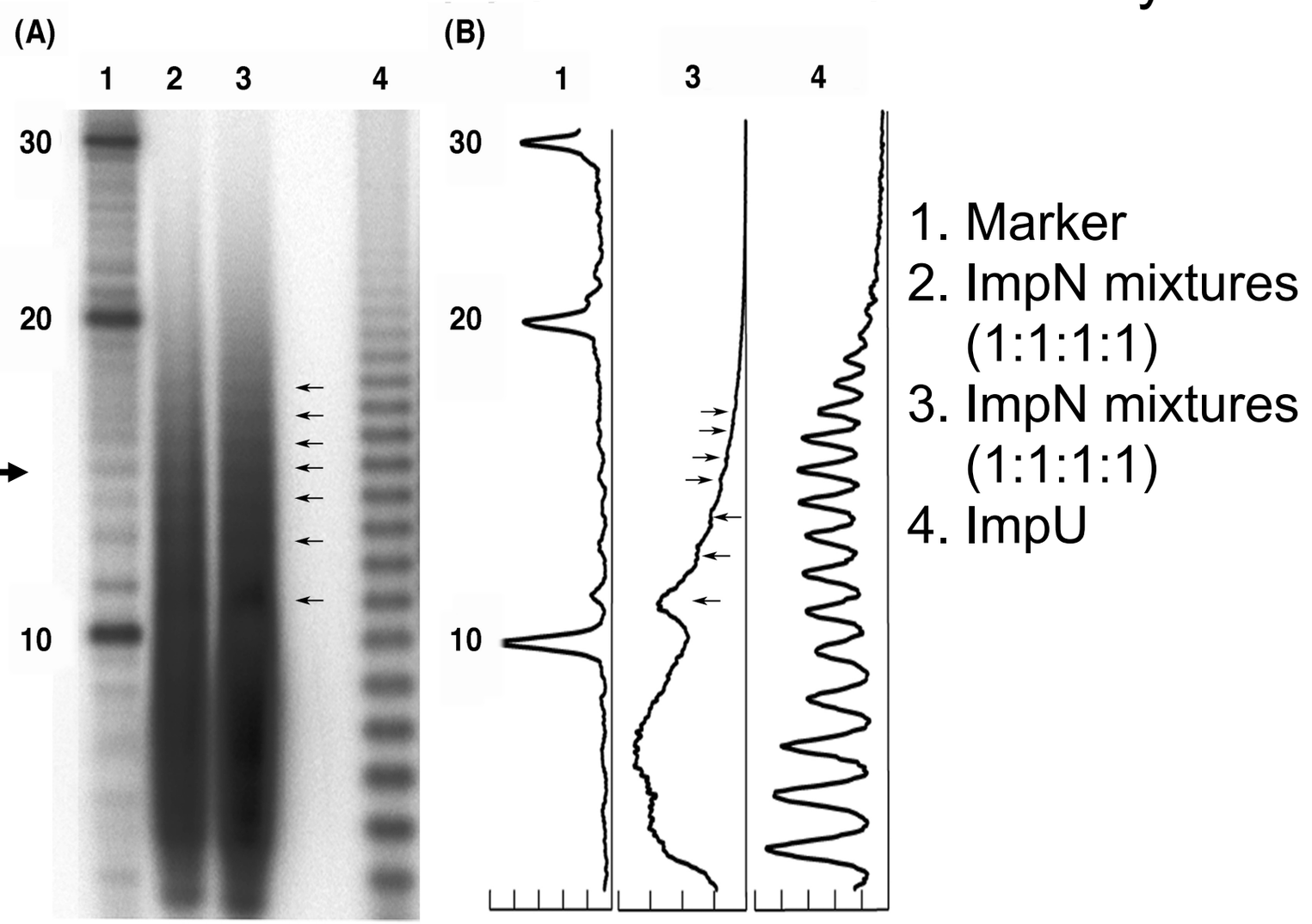
Self-condensation of monomers

Samples: < 5 mM activated monomers (ImpN), < 5.2 mM Mg(II), < 0.6 mM Pb (II)
Preparation: Mix @ 25 ˚C, freeze and maintain @ -18 ˚C for up to 40 days.



Mg^{2+}/Pb^{2+}

Freeze

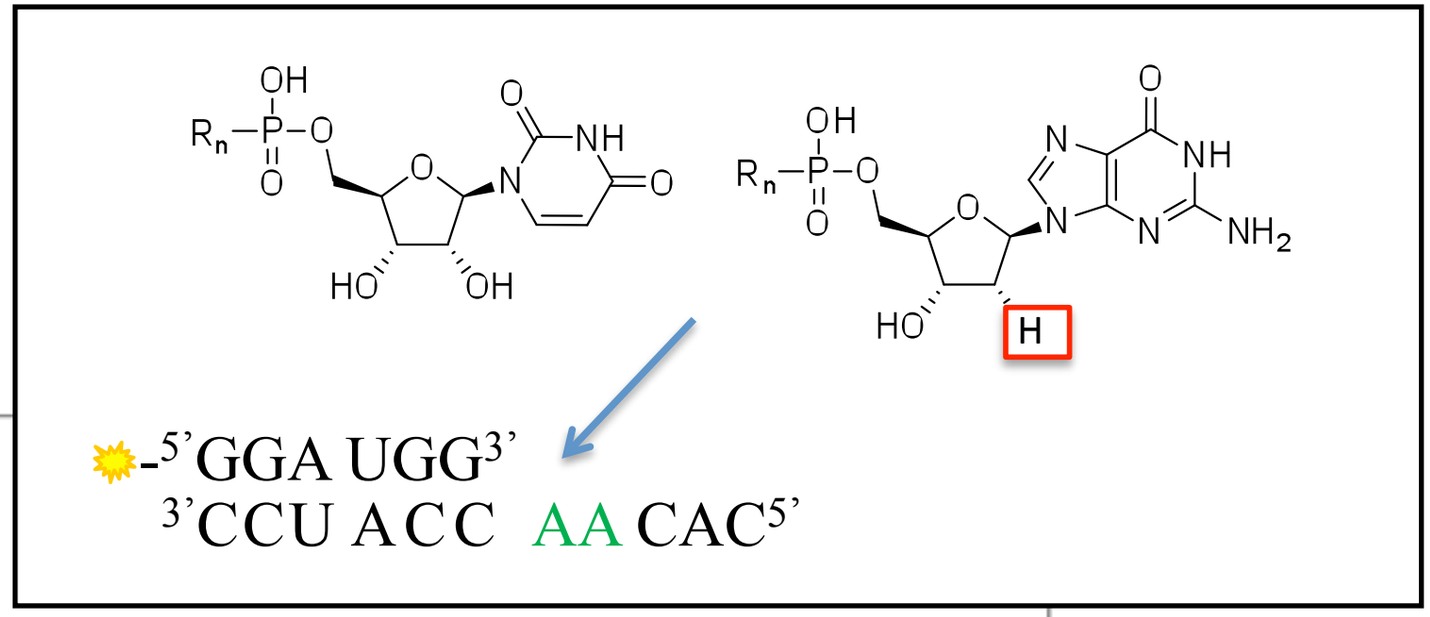


1. Marker
2. ImpN mixtures (1:1:1:1)
3. ImpN mixtures (1:1:1:1)
4. ImpU

All mixtures tested same average yields (>80% incorporation, 50% ≥ 3-mer, up to 15- to 22-mer, equal incorporation of all nucleobases in mixed products, more 45% oligomers with 3´-5´)

Kanavarioti et al 2001 Astrobiology; Monnard et al 2003 J. Am. Chem. Soc

Non-enzymatic, template-directed polymerization: Steps towards self-replication



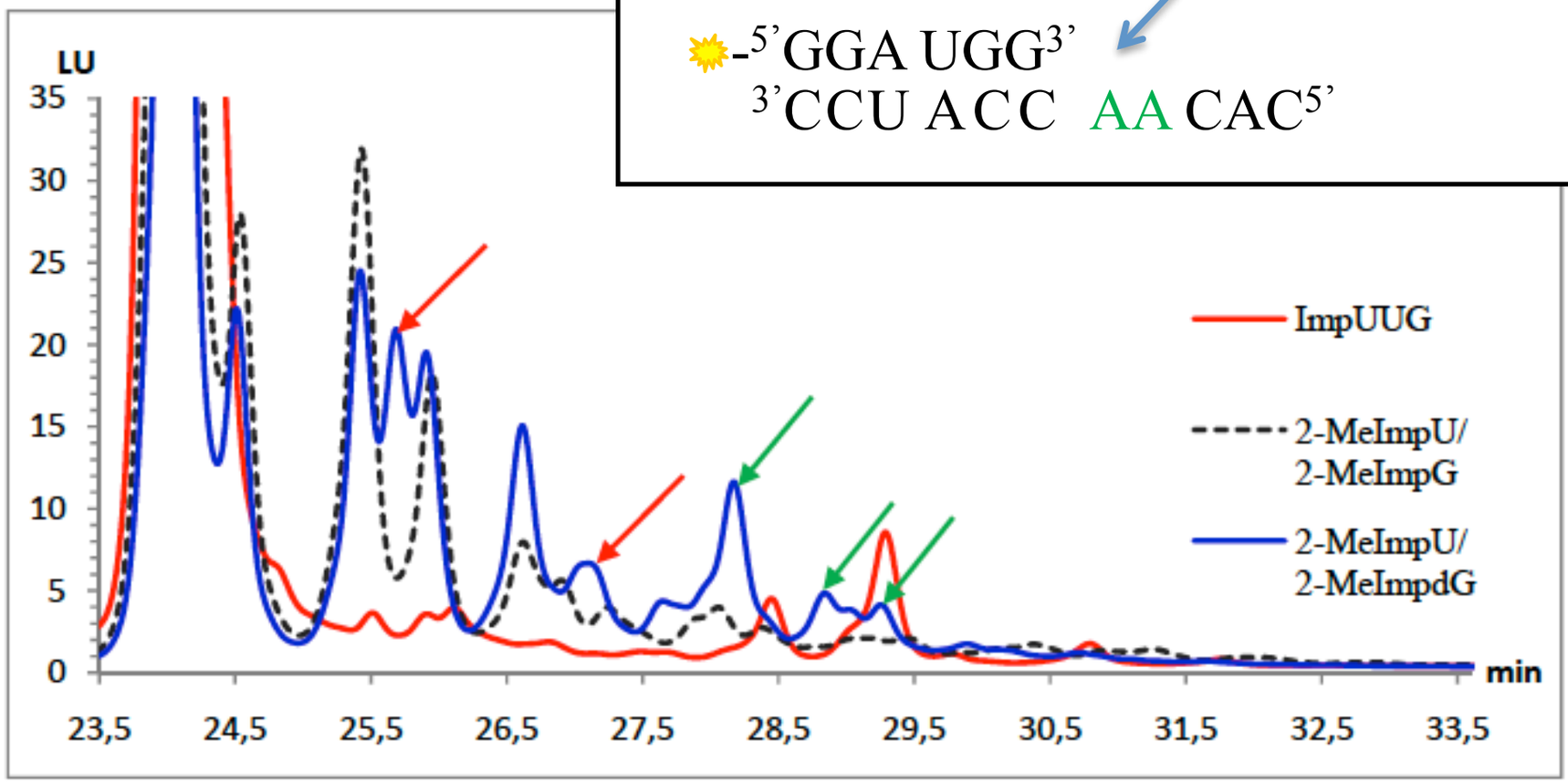
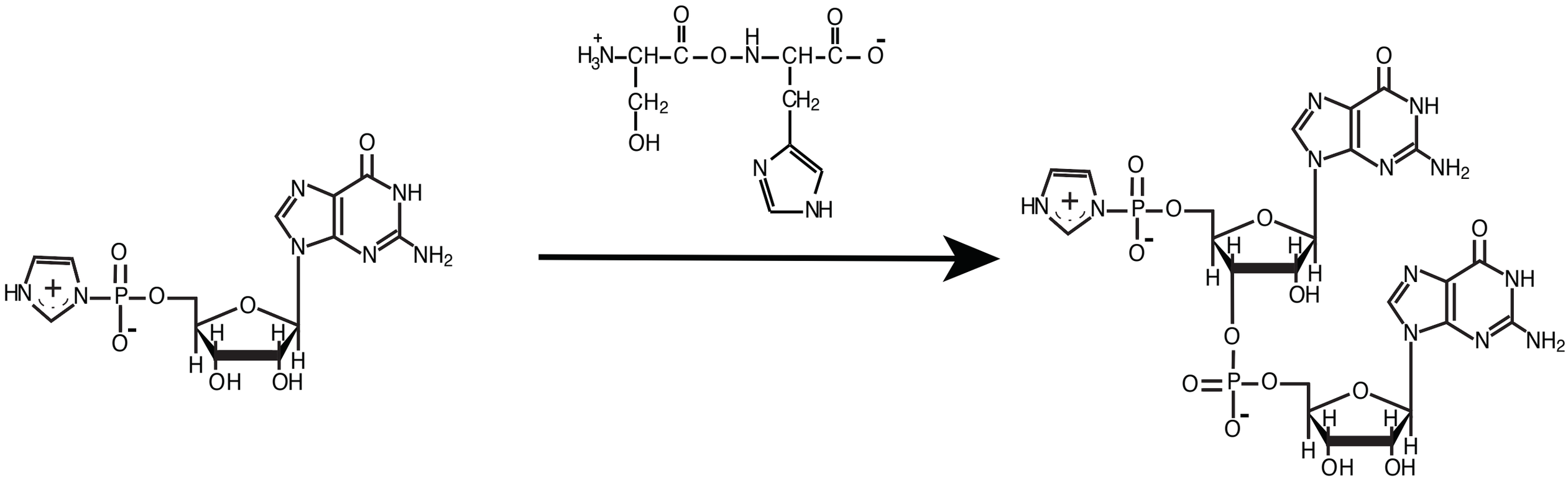
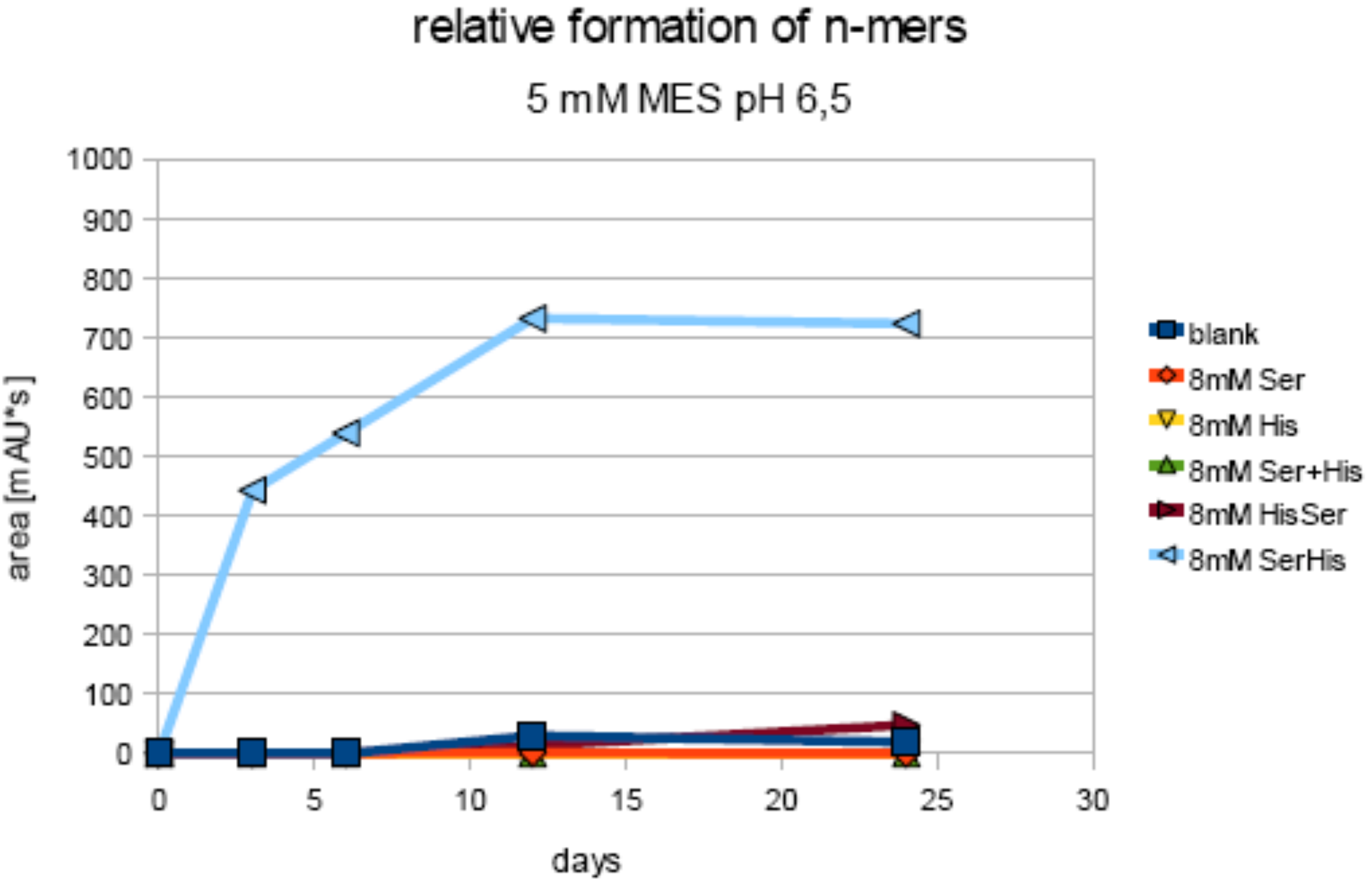


Figure 2.7-3: Experiment with 2-MeImpdG. *An overlay of the chromatograms of the UUG ligation (**PL17**, red, 5d) with the experiment where dG was employed to "cap" the primer or its primer+$(U)_n$ elongation products. (**PL18**, blue). As a reference the analysis of the reaction with a ribonucleotide G is overlaid. (black, stipled). See text for the explanation of red and green arrows. Reactions were incubated at -18.4° C for 14d, using 1.75mM 2-MeImpU and 0.6mM 2-MeImpdG or 2-MeImpG in the presence of **chim-P** and **t#U**.*

Emergence of peptide catalysis



Rafał Wieczorek


relative formation of n-mers
5 mM MES pH 6,5
area [mAU*s]
1000
900
800
700
600
500
400
300
200
100
0
0
5
10
15
20
25
30
days
blank
8mM Ser
8mM His
8mM Ser+His
8mM HisSer
8mM SerHis

How to handle the research in the Origin of Life fields:

What do we still need to understand this emergence?

- Chemical composition
- Plausible pathways and reaction networks
- Sequence of events (i.e., the transitions)

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What do we still need to understand this emergence?

- Chemical composition
- Plausible pathways and reaction networks
- Sequence of events (i.e., the transitions)

Is it sufficient to study one aspect? (development of membranes, polymer based genetics and catalytic system...)

- Necessary to understand each aspect/component by itself but not sufficient
  - ➡ Systemic approach to the problem (system chemistry)
  - ➡ Less attachment to specific molecules and more considerations on classes of molecules and processes that are plausible with them.
  - ➡ Computing support (simulations, numerical analysis) to allow deconvolution of the complex interactions that exist in complex chemical systems.
  - ➡ Perhaps shift of paradigms is necessary: co-evolution of the various components of early living systems. Acceptance of sub-optimal yields (i.e. conditions for a given reaction) and perhaps unusual functions of some components (compared to today biology)

Acknowledgements

Collaborators

Dr. J. A. Bailey (LANL, scientist)

Dr. J.M. Boncella (LANL, scientist)

Dr. H.-J. Ziock (LANL, scientist)

Dr. S. Rasmussen (SDU, Prof.)

Dr. D. W. Deamer (UCSC, Prof.)

Dr. K. A. Nielsen (SDU, assistant Prof.)

Dr. P.L. Luisi (Roma Tre, Prof.)

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Dr. M. Dörr (SDU)

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P.L. Pedersen (SDU, Ph.D.)

A. Albertsen (SDU, Ph.D.)

P.M.G. Löffler (SDU, Ph.D.)

T. E. Rasmussen (SDU, MS)

A. Zebitz Eriksen (SDU, BSc)

Funding

LDRD program (LANL) (past)

NASA (current, NNH08AI881)

EU commission: MATCHIT (FP7)

Danish National Science Foundation (current)

University of Southern Denmark (current)