The Origin of Life
and the
Emergence of Darwinian Evolution

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Bacteria

You are here -->

Eucarya

Archaea

Slide courtesy of Norm Pace
Organizational Complexity of Modern Life

DNA → replication → RNA → proteins → Structure and function

DNA processing

RNA processing
A great simplification:

RNA

expression

biochemical functions

replication
How did we get to the RNA World?

small molecules (CO, H₂, H₂O, NH₃, CH₄…) + energy

- lipids + sugars + nucleobases + high-energy + amino acids

- cofactors

- activated nucleotides

- Self-assembly into vesicles

- Assembly into genetic polymer

- peptides

- protocell?
Nucleoside triphosphates

Very polar
Low membrane permeability
Low chemical reactivity

Nucleoside phosphorimidazolides

Less polar
High membrane permeability
High chemical reactivity
(faster polymerization, hydrolysis and cyclization)
Polymerization of ImpNs on Clay

Polymerization of ImpNs in an Ice Eutectic Phase

Spontaneous primer-extension

5'-r-GCUGCCAGUG
3'-d-CGACGGTCAC-C-CCTTGAG

5'-r-GCUGCCAGUG
3'-d-CGACGGTCAC-C-CCTTGAG

2-MeImpG
MgCl₂

5'-r-GCUGCCAGUG-GGG
3'-d-CGACGGTCAC-C-CCTTGAG

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Current state-of-the-art in RNA-catalyzed RNA replication: A 2-domain ribozyme polymerase from the Bartel lab.

Replicases copying random templates in solution
Random segregation within compartments

A simple cell based on a replicating vesicle for compartmentalization, and a replicating genome. A complex environment providing nucleotides, lipids and various sources of energy...

...such as phase transfer and osmotic gradient energy (for growth), mechanical energy and ion gradients (for division), and chemical energy (for nucleotide activation).
Myristoleate Vesicles

Fatty acid structures depend upon pH

$\Delta pH$

$\text{pH} \geq 10$

$\text{Micelles}$

$\text{pH} \sim 8.5$

$\text{Liposomes}$

Fatty acid structures depend upon pH
PL-dyes do not exchange between FA vesicles
Myristoleate Vesicles Retain Encapsulated RNA
Spontaneous Assembly of Oleate Vesicles
Montmorillonite Clay Accelerates Membrane Formation from Micelles

Since oligonucleotides can be synthesized on clay surfaces, clay-catalyzed vesicle assembly provides a direct path for the incorporation of oligos into vesicles.

0.2M Na⁺-bicine, pH 8.5, 25°C; +/- 0.05mg/mL Na⁺-montmorillonite; 10mM myristoleate added after 2mins.
Montmorillonite become Encapsulated in Liposomes

Clay:Nomarski Optics

Vesicles; Fluorescence Filter
Montmorillonite can bring RNA into Vesicles
Montmorillonite can bring RNA into Vesicles
Montmorillonite can bring RNA into Vesicles
Spontaneous Vesicle Growth

was first demonstrated by the Luisi lab in the ETH, Zurich, Switzerland

Addition of 5 mM oleate to 0.2 mM POPC vesicles

A FRET-based assay for lipid incorporation

Donor: NBD-DHPE

Acceptor: Rh-DHPE

Addition of 1 equivalent of micelles over 4 hours

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Division by Extrusion

Input of mechanical energy by pore-extrusion causes division

Some contents are lost - but there is little if any dilution
Cycles of growth and division

Growth and Division (mean size)
Darwinian evolution at the cellular level: Vesicle Competition
Osmotic Pressure: A link between genome replication and vesicle growth?

Internal osmotic pressure tensions and stretches the membrane, exposing hydrophobic surface area, and favoring the capture of new lipid molecules.
Vesicle competition
Swollen vesicles labeled

Osmolyte: tRNA    membrane: MA-GMM.
Vesicle competition
Isotonic vesicles labeled

Osmolyte: tRNA    membrane: MA-GMM.
Osmotically Driven Membrane Growth

High Internal Concentration of Nucleic Acid

↓

Faster Membrane Growth

Osmotic pressure creates membrane tension...

...which relaxes as the membrane grows.
Alternative Nucleic Acid Backbones

DNA

TNA

GmNA

GNA

NP-DNA

NP-TNA

NP-GmNA

NP-GNA
Phosphoramidate DNA

3’-amino-2’,3’-dideoxy-guanosine-5’-phosphorimidazolate (3’NH₂ImpdG)

- RNA-like structure: 3’ endo sugar, A-type helix
- Forms duplexes with complementary DNA, RNA and NP-DNA.
- Greater nucleophilicity of the 3’-amino vs. 3’-hydroxyl leads to faster spontaneous polymerization.
- Phosphoramidate bonds may also link other backbones (e.g. threose, glycerol, methoxyglycerol).
Summary of Progress

- Multiple pathways for vesicle growth and division
- Nucleotides can diffuse into vesicles
- Ribozymes active inside vesicles
- Chemical approach to nucleic acid replication looks promising, bypassing need for complex ribozyme
What have we learned that is relevant to the Origin of Life?

- Simple but unexpected physical phenomena may play a variety of important roles
  - Selective sugar permeability favoring ribose
  - Osmotic pressure driving vesicle growth
- Mineral particles may help to bring components together
- Simple membranes are surprisingly robust
- Energy dissipated in interesting ways
  - Chemical energy in activated nucleotides does osmotic work
  - Phase transition energy in membrane growth leads to pH gradients
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