The Origin Of Life: A Network Oriented View

Attractor Based Evolution

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Presentation Objectives And Outline

Objectives

- Introduce the metabolic hypothesis for the origin of life
- Set out a Network Oriented view of chemistry
- Spell out explicitely a mechanism for inheritance in attractor based (non template) evolution
- Focus on the *logical structure* of the problem[a]
- SimSoup update
- OOL is a multidisciplinary subject; present accordingly
- Discussion

[a] Don't be prescriptive about whether early life was based on RNA, protein, lipids, or something else.

Outline

- See left

Introduction

Section Outline

- Key Issues for the Origin Of Life
- The Metabolic and Genetic Views
- The Conceptual Background For SimSoup
- Metabolic Hypothesis

Introduction
Origin Of Life Issues

Key Questions

- **Trophic Method:** What were the first evolving systems built from (what did they eat)?
- **Homochirality:** How did this arise?
- **Individuation:** How were individual organisms separated from one another?
- **Origin of Evolution:** How did entities capable of transferring inherited information arise?

Introduction
Metabolic And Genetic Views: Genetic

The RNA World

- **Accurate template replicators are needed:** The extreme improbablity of such molecules arising by random processes is a major difficulty for the RNA World. (Eigen's chicken and egg paradox)
- **A ready supply of homochiral monomers is needed:** The macro-molecules of life cannot be constructed in the presence of monomers of mixed chirality

Cairns Smith's Clay Crystals

- Deals with homochirality...
- But must show inheritance in clay based organisms...
- And that genetic takeover can take place

Introduction
Metabolic And Genetic Views: Metabolic

Metabolic View: Advantages And Key Challenges

- Life can start simple...
- No need for accurate template replicators
- No need for a ready supply of homochiral monomers
- In autotrophic variants, only an energy supply and low molecular weight molecules are neededf

Key Challenges

- Identify and explain an inheritance mechanism
- Explain individuation and reproduction
- Explain how genetic takeover ocurred

Relevant Work And Concepts

- The Metabolic View theories of Aleksandr Oparin, Stuart Kauffman, Freeman Dyson
- The Lipid World and the GARD model of Doron Lancet's group (recently criticised by Vasa, Szathmáry and Santos)
- Network theory, particularly the work of Sanjay Jain and Sandeep Krishna
- Günter Wächtershäuser's chemo-autotrophic Iron-Sulphur World
- Linus Pauling: The Nature Of The Chemical Bond
- Tibor Gánti: Principles of Life, Fluid Machines, Chemoton
- Formose reaction based lipid encapsulated protocell of Ben Davis' group
- Chrisantha Fernando: Origin of informational replicators[a]
- Organisation Theory: Peter Dittrich and Pietro Speroni di Fenizio
- Individuation: Bénard Cells, Spots (Nathaniel Virgo)

[a] Also recent paper by Fernando and Vasa on co-optive evolution in chemical networks

Evolution Of Metabolic Networks

- Evolution is essentially a process of trial and error
- Successful trials must be inherited. That is, remembered and transmitted to offspring
- **Hypothesis:** Early organisms contained chemical networks that were capable of carrying and passing on inherited information
- Intuitive Argument: There are many examples in which networks are known to carry information. The most striking is the brain

Chemistry: A Network View

Section Outline

- Elements Of A Chemical Network
- Mathematical Networks
- Static And Dynamic Chemical Networks
- Catalysis
- Network Memory And exploration
- A Four State Artificial Chemitry That Builds Polymers

Chemistry: A Network View
Network Elements

What Are The Basic Units Of A Chemical Network?

- Chemistry is about particles and reactions
- The particles can be molecules or ions and are of many different types
  - SimSoup term: *Molecule Type*
- The reactions are of many different types
  - SimSoup term: *Interaction Type*
- To understand chemistry as a network, we must be able to represent:
  - Molecule Types
  - Interaction Types

Chemistry: A Network View

Network Elements: Molecule Types

What Is A Molecule Type? (SimSoup Terminology)

- Molecule Type:
  - A possible assembly of Atom Types
  - A Molecule Type has structure (more later...)
- Atom Type:
  - An indivisible Molecule Type
  - Can correspond to an element in real chemistry, but does not have to[a]

[a] An Atom Type could be used to model a chemical group provided that it does not split under the conditions of interest

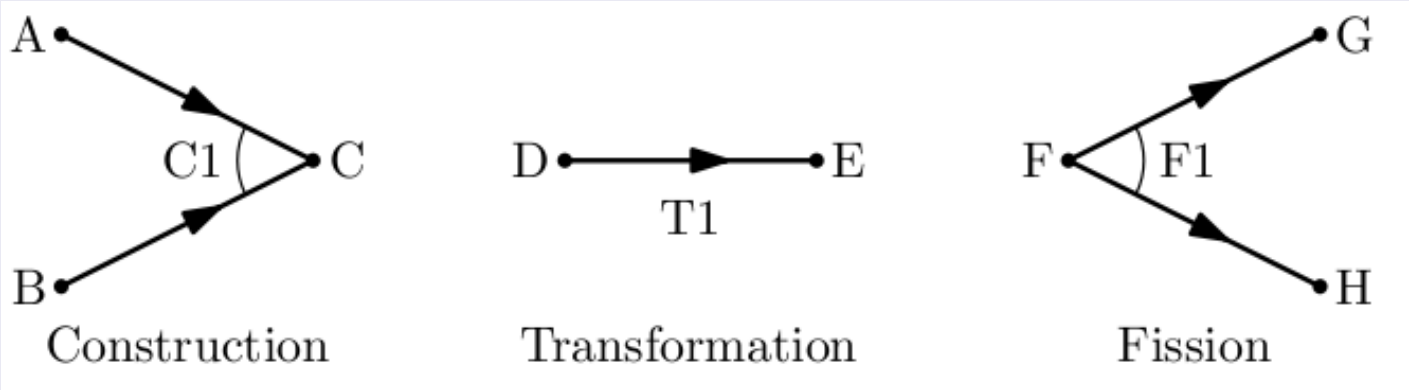
Representing Molecule Types In A SimSoup Network

- Molecule Types are represented as Nodes
- Each Node represents a different Molecule Type

Chemistry: A Network View

Network Elements: Interaction Types

Three Forms Of Interaction



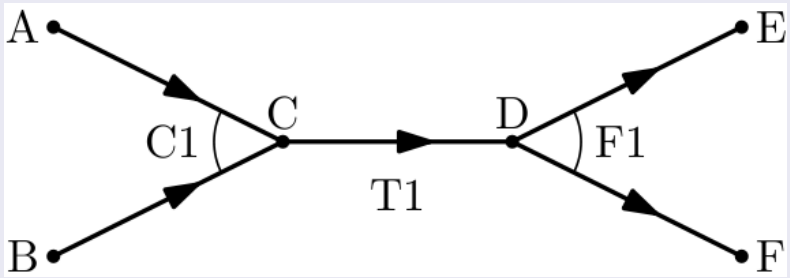
$A + B \rightarrow C$ $D \rightarrow E$ $F \rightarrow G + H$

- Only three things can happen in chemistry:
  - Construction: Two Molecules join
  - Transformation: A Molecule re-arranges
  - Fission: A Molecule splits
- All more complex Interactions are combinations of these three elementary interactions

Chemistry: A Network View

Network Elements: Compound Interactions

Compound Interactions

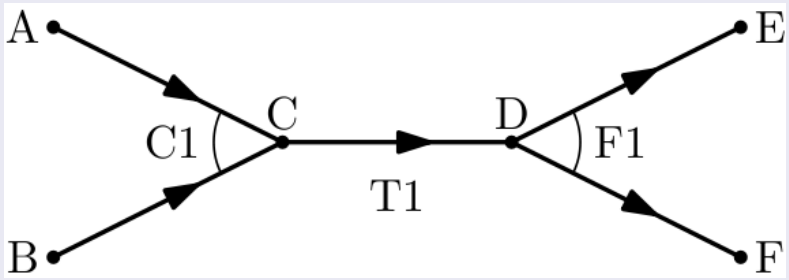


The above is a Compound Interaction with overall scheme $A + B \rightarrow E + F$

A Compound Interaction Does Not Have A Rate Constant

- Rate depends on the concentrations of C and D
- In a larger network, C and D may be reactants or products for other Interaction Types...
- ... A Compound Interaction cannot be modelled as a type of reaction with a rate constant

Bipartite Graphs and Hypergraphs



- Graph: A set consisting of Nodes, and Edges connecting pairs of Nodes
- A chemical network is *not* a Graph with Molecule Types as Nodes and Interaction Types as Edges
  - Construction C1 above has three connected Nodes...
  - ... it cannot be represented as two separate Edges
- A chemical network is a *directed hypergraph*[a]
- Or equivalently a *bipartite directed graph* in which both Molecule Types and Interaction Types are Nodes[b]

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[a] A hypergraph is a generalisation of a graph, where a 'hyperedge' can connect any number of vertices. In a directed hypergraph, hyperedges connect 'head' nodes to 'tail' nodes.

[b] A bipartite graph has vertices that can be divided into two disjoint sets U and V such that every edge connects a vertex in U to one in V. In a bipartite directed graph, each edge has a direction.

Chemistry: A Network View

Static And Dynamic Chemical Networks

The Static Network

- Is defined by:
  - Molecule Types
  - Interaction Types
  - Rate constants (temperature & pressure dependent)
- Is determined for all time by the laws of physics
- Is infinite in real chemistry (because no upper limit to Molecule size)

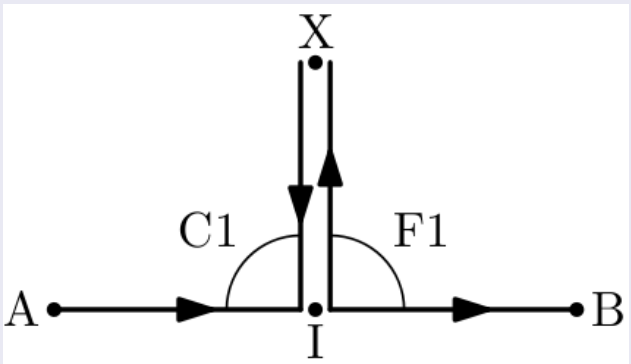
A Dynamic Network

- Consists of:
  - Actual Molecules
  - Actual Interactions taking place between them
  - Actual Interaction rates
- Is a possible configuration on the Static Network

Chemistry: A Network View
Catalysis

Catalysis: Process Oriented View

- 'Catalyst' is not a kind of Molecule
- It is a *role* that a Molecule can play in a chemical process
- In this example, X plays the role of catalyst

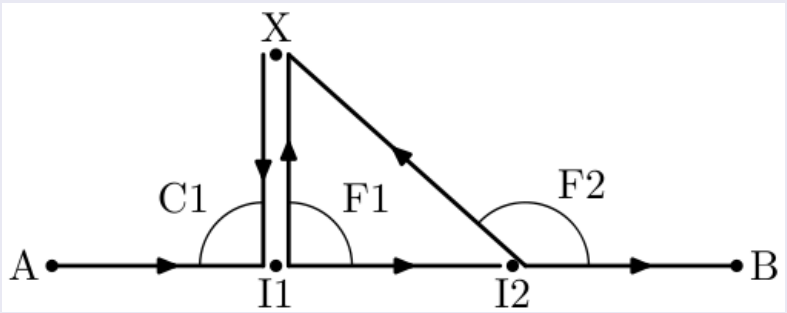


$$A + X \rightarrow I$$
$$I \rightarrow X + B$$

Chemistry: A Network View

Network Memory And Exploration: Two State Memory Unit

A Chemical Network That Can Remember



$$A + X \rightarrow I1 \quad (C1)$$
$$I1 \rightarrow X + I2 \quad (F1)$$
$$I2 \rightarrow X + B \quad (F2)$$

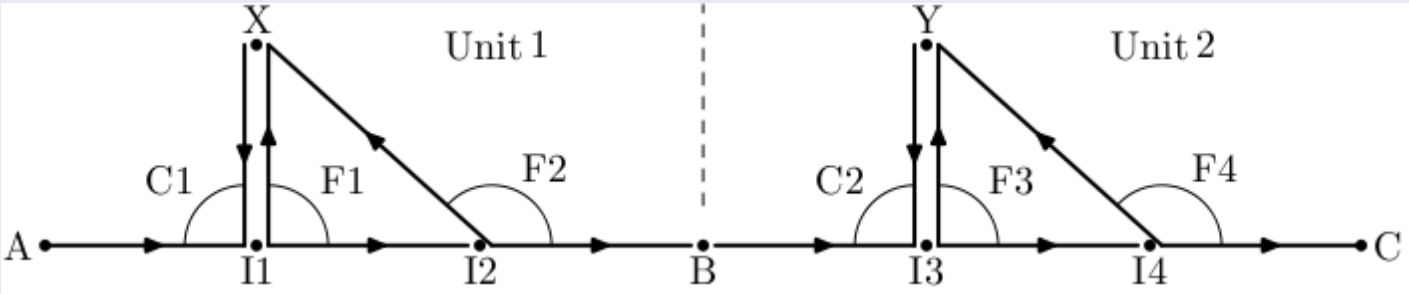
- Overall Scheme: $A \xrightarrow{X} B + X$
- Assume A is ‘food’ with fixed concentration
- The process is autocatalytic
- There are two stable states [a]:
  - ‘Inactive’: X is not present
  - ‘Active’: X is present and *maintained*
- The active state is an *attractor* - concentrations are restored if perturbed
- Addition of a single Molecule of X to an inactive network is remembered

[a] Assume a small leakage of Molecules from the reactor

Chemistry: A Network View

Network Memory And Exploration: Network Exploration

A Network With Memory Can Be Explored

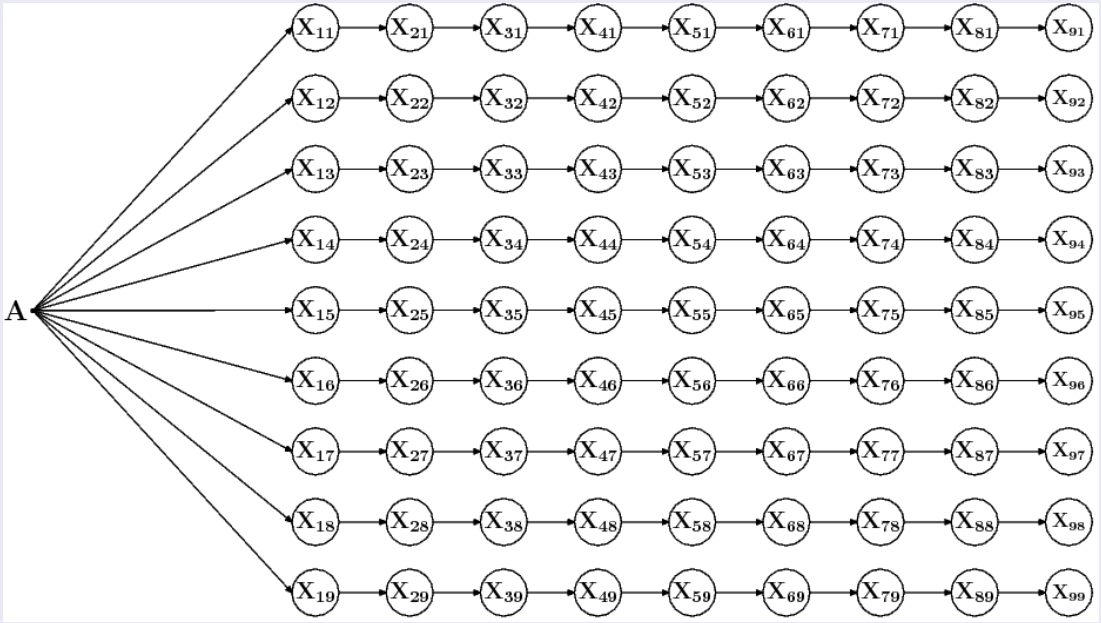


- The network has three stable states
  - State 1: Inactive
  - State 2: Unit 1 only active
  - State 3: Units 1 and 2 active
- State 3 can only be reached via State 2
  - First perturb by adding one Molecule of X
  - Then add one Molecule of Y
- In a large network, successive perturbations will lead to a process of exploration and discovery

Chemistry: A Network View

Network Memory And Exploration: A Memory Bank

An Artificial Chemistry With Many Attractors



- Autocatalytic two-state sub-networks (memory units) with catalysts X_{ij}
- A is food for the first column units
- Each unit produces food for the next
- Each row has 10 attractors (from all units inactive to all units active)
- The rows can be explored independently
- The network as a whole has 10^9 distinct attractors

Chemistry: A Network View

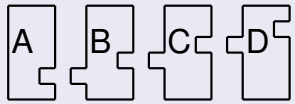
A Polymer (Artificial) Chemistry With Four Stable States

Food Set

- A - a 'monomer'. BB, CC and DD are 'stable' dimers that can be cleaved under specific conditions

Reactions That Make A New Dimer

- $A + B \longrightarrow AB$ // A can *not* join with A, C or D. Eg due to incompatible shapes:



- $AB + BB \longrightarrow \begin{matrix} AB \\ BB \end{matrix}$
- $\begin{matrix} AB \\ BB \end{matrix} \longrightarrow \begin{matrix} AB \\ B \end{matrix} + B$ // The dimer is cleaved to return the catalyst
- $\begin{matrix} AB \\ B \end{matrix} \longrightarrow AB + B$ // Excess catalyst ensures stability
- Overall Scheme: $A + BB \xrightarrow{B} AB + B$

Continuing the Polymer

- $AB + CC \xrightarrow{C} ABC + C$ // AB can *not* join with A, B or D
- $ABC + DD \xrightarrow{D} ABCD + D$ // ABC can *not* join with A, B or C

The Chemistry Has Four Alternative Stable States

- Four alternative stable states: Food + ({∅} or {AB} or {AB, ABC} or {AB, ABC, ABCD})
- Requirement: BB, CC and DD are stable, but can be cleaved by (only) AB, ABC, ABCD respectively

Attractor Based Evolution

Section Outline

- What Is Envisaged?
- Open Questions - How Many Attractors?
- More Open Questions

Attractor Based Evolution
What Is Envisaged?

Scenario For Attractor Based Evolution

- Metabolism first theories usually assume that
  - Early organisms had a means for individuation
  - They could divide and produce offspring
- Recall: The static network in real chemistry is infinite
- **If** memory and exploration as illustrated is supported...
- ... and the molecular composition of each offspring is roughly similar to that of the parent, then ...
- ... new sub-networks discovered by the parent will be retained by the offspring *because they are attractors*
- ... and evolution will occur
- Lamarckian (non-Darwinian) evolution, because aqcuired characteristics are inherited

Network Evolution
Open Questions

What Kind Of Network Supports Many Attractors?

- The memory bank example can be extended to support an unlimited number of attractors...
- ...But the example was specifically designed
- Can real chemical networks support many attractors?[a]
- What network properties result in many attractors?
  - Many Molecule Types? Few Molecule Types?
  - High connectivity? Low connectivity? Small World?
  - Do simplifying constraints of some kind help?[b]
  - ...

[a] Vasas, Szathmáry and Santos - PNAS paper, say “Information in attractor-based systems crucially depends on the limited number of alternative stable states...”, but that is based on analysis of a GARD system with a fixed number of Molecule Types, a finite network with random connectivity, and simplifying assumptions enabling the network to be represented as a graph

[b] For example, as in the memory bank with independent ‘rows’

Network Evolution
More Open Questions

More Open Questions For Network Evolution

- How many attractors are needed to provide a scaffold for genetic takeover?
- How frequent are transitions between attractors?
- What causes them?
- What mechanisms could support individuality and reproduction in non template replicating organisms?
- How could the transition to template replicators (Genetic Takeover) be made?
- What is the relationship between molecular structure and chemical network structure?

SimSoup

Section Outline

- Basic Network Simulator
- SimSoup Extended As A Network Explorer
- Preliminary Results

SimSoup
Basic Model

SimSoup As A Network Simulator

- Static Network
  - Setup Molecule Types and Interaction Types (Constructions, Transformations and Fissions)
  - Each Interaction Type must conserve Mass
  - Rate constants are themodynamically realistic
- Network Dynamics
  - Interactions occur in a well stirred Reactor
  - Interaction Rates
    - Bimolecular Interaction Types - k[R1][R2]
    - Unimolecular Interaction Types - k[R1]

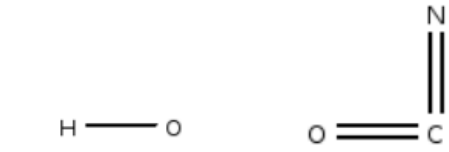
SimSoup
Extended Model

SimSoup Extended As A Network Explorer

- Molecule Types and Interaction Types not pre-defined
- Adding molecular structure allows a more open-ended approach
  - Each Molecule Type has a two dimensional structure, built from Atoms
  - Molecules can Join or Split to form Molecules of different types
  - Rules analogous to real chemistry, but simple
    - Joining: According to valence rules. Maximize total bond energy. Atoms cannot overlap
    - Split: Break bonds with least total energy
- Opportunities for novelty and exploration

SimSoup
Preliminary Results

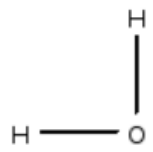
Molecules Constructed By SimSoup



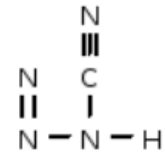
(a) $N_{Mols} = 93$

(b) $N_{Mols} = 64$

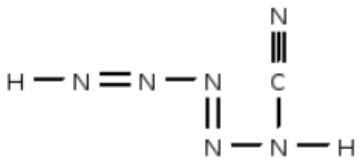
(c) 'Hydrogen Cyanide' $N_{Mols} = 43$



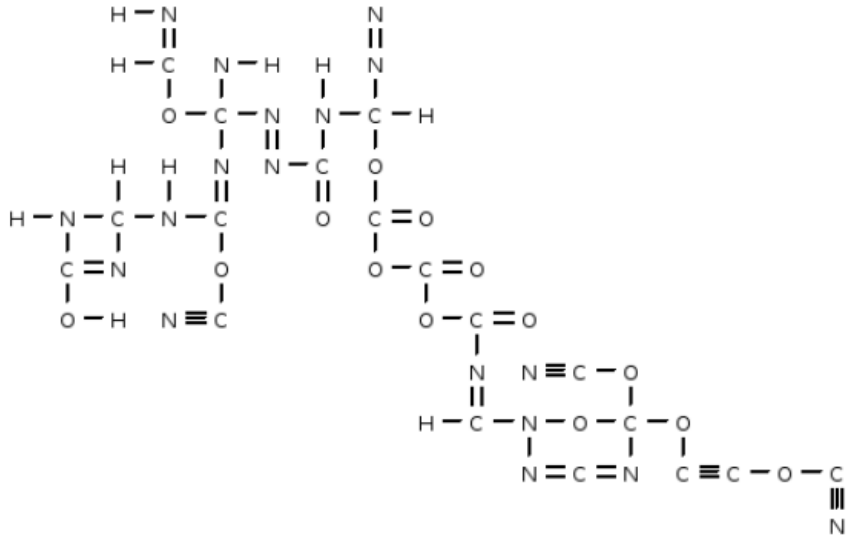
(d) 'Water' $N_{Mols} = 33$



(e) $N_{Mols} = 6$



(f) $N_{Mols} = 4$



(g) $N_{Mols} = 1$

Conclusion

Conclusions and a Question

- Artificial chemical networks with appropriate network connectivity can support an unlimited number of stable attractor states
- Such states in *artificial* networks could form the basis of an inheritance mechanism to support evolution[a]
- It is unknown how many attractor states can be supported by real chemical networks
- SimSoup forms a platform for simulating open-ended exploration of chemical networks in which ...
- ... chemical network structure is determined by molecular structure
- Can a set of real molecular species that supports attractor based evolution be identified?

[a] Individuation and a means of reproduction would also be required

Questions

Questions?