SimSoup: An Artificial Chemistry Model for the Investigation of the Evolution of Metabolic Networks

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http://www.simsoup.info/Publications.html

SimSoup: An Artificial Chemistry Model for the Investigation of the Evolution of Metabolic Networks

- The Origin Of Life - Background Topics
- Motivation for SimSoup
- The Physics of the SimSoup Model
- Compound Interactions
- Catalysis in SimSoup
- Inheritance: A Compound Interaction that can Remember
- Preliminary SimSoup Scenarios
- Conclusions and Prospects

The Origin Of Life - Background Topics: The Genetic and Metabolic Views

- The Genetic View
  - Template replicating molecules or crystals were crucial for the Origin of Life
    - RNA World
    - Cairns-Smith
- The Metabolic View
  - The first living entities were metabolic systems
    - Oparin, Kauffman, Dyson, Segré et al., Jain and Krishna
- Alternative Categorisation of Views: Wächtershäuser
  - First life was Heterotrophic: Primordial Soup
  - First life was Autotrophic: Eg Iron Sulphur World

The Origin Of Life - Background Topics: Key Issues

- **Homochirality:** The macro-molecules of life (eg proteins, DNA, RNA) are constructed from sub-units with uniform ‘handedness’

There is currently no accepted explanation for this

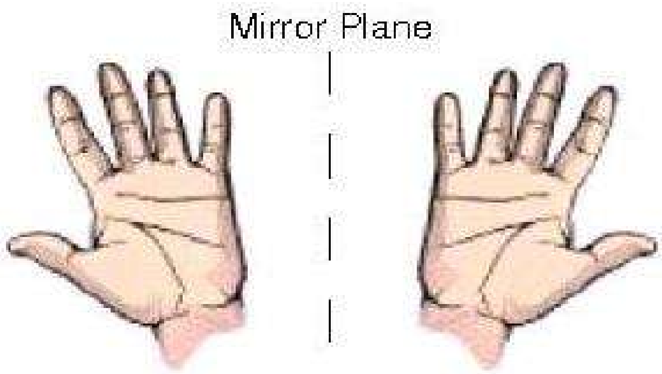
- **Transfer of Hereditary Information:** Essential for evolution

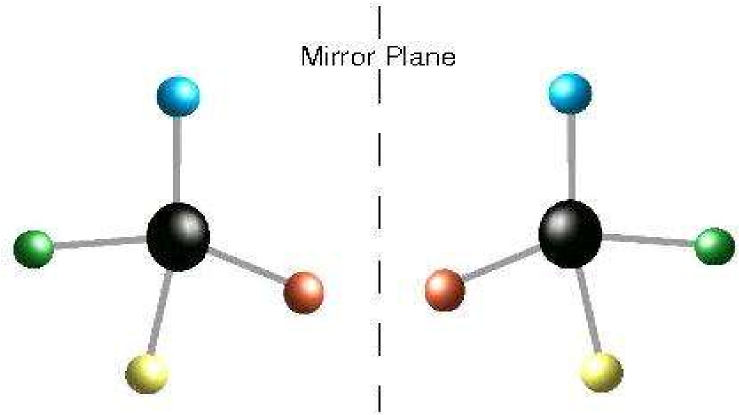
Contemporary template replicators need highly sophisticated error correction mechanisms. But how did these evolve without template replicators to carry hereditary information?

Chicken and egg problem (Eigen’s Paradox)

The Origin Of Life - Background Topics: Homochirality/1

- Left and Right Handed (Chiral) Objects





- The Macro-Molecules of Life are Homochiral
  - Most everyday objects are chiral
  - All amino acids (except glycine) are chiral
  - But in proteins, only L type amino acids are found
  - Similar point applies to DNA / RNA
  - Why? And how did this arise?

Homochirality/2

- Homochirality of DNA and proteins is a necessity: Structure is crucial
- The macro-molecules of life cannot be constructed from sub-units of different chirality
  - “monomers of opposite handedness to the template are incorporated as chain terminators … This inhibition raises an important problem for many theories of the origin of life”
  - From Joyce, G.F., Visser, G.M., van Boeckel, C.A.A., van Boom, J.H., Orgel, L.E. and van Westrenen, J., Chiral selection in poly(C)-directed synthesis of oligo(G) Nature -1984 .
- What was the origin of chiral discrimination?
- Bonner Hypothesis - Extraterrestrial origin
  - William Bonner – mid 1990s: “I happen to think that you have to understand the origin of homochirality before you can bridge that gap [to the Origin of Life]. Stepwise, one has to deal with the origin of homochirality first, and then how do you get to living organisms... I spent 25 years looking for terrestrial mechanisms for homochirality and trying to experimentally investigate them and didn't find any supporting evidence”

The Origin Of Life - Background Topics: Transfer of Hereditary Information/1

- Transfer of Hereditary Information
  - Inheritance requires transfer of information determining the nature of offspring: Beneficial characteristics discovered by evolution must be remembered and passed on
- The Error Threshold
  - Contemporary life uses highly evolved error correction mechanisms
  - Without such mechanisms, RNA template replicators with more than 100 bases cannot copy reliably

The Origin Of Life - Background Topics: Transfer of Hereditary Information/2

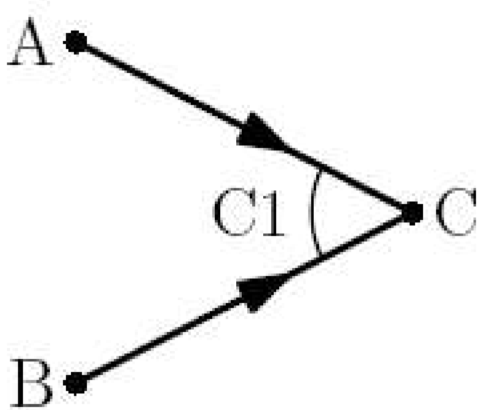
- Eigen's Paradox
  - Without error correction machinery, the maximum size of a naked gene replicator is about 100 bases
  - In order for a genome to specify an error correction machinery, it must be substantially larger than 100 bases
  - Chicken and egg problem.

Motivation for SimSoup

- **Primary:** To provide an abstract model of chemical networks and a framework for investigating the dynamic properties of such networks, especially in regard to inheritance mechanisms relevant to the beginning of evolution and the Origin of Life
- **Secondary:** To provide a network modelling tool suitable for many other types of network

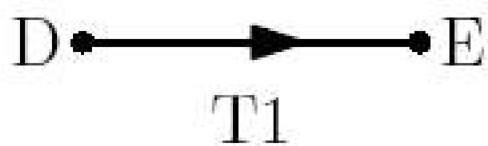
SimSoup Physics: The Static Model

- Molecule Types:-
  - Analogous to particles that interact in real chemistry
  - This includes molecular species, but can also include unstable intermediates
  - Each Molecule Type has a defined mass
- Interaction Types (Only three!)



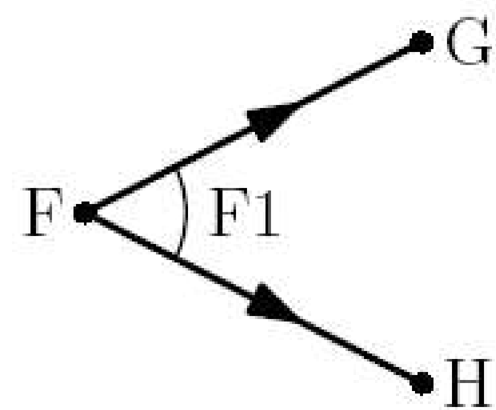
Construction

A + B → C



Transformation

D → E



Fission

F →G + H

SimSoup Physics: The Dynamic Model/1

- Reactor: An enclosed space containing Molecules
- Molecule: An instance of a Molecule Type
- Realisable Interaction Type: An Interaction Type that is currently possible in the Reactor
- Interaction Rate:-
  - Construction $A + B \rightarrow C$ kab - Second Order
  - Transformation $D \rightarrow E$ kd - First Order
  - Fission $F \rightarrow G + H$ kf - First Order
  - *k is the Rate Constant for an Interaction Type*
  - *a is the concentration of Molecule Type A*

SimSoup Physics: The Dynamic Model/2

- Model Operation
  - At each timestep:-
    - Execute any Action Requests for this timestep (eg to add perturbation Molecules)
    - For each Realisable Interaction Type:-
      - Determine number of Interactions this timestep
      - Remove Reactant Molecules and Add Product Molecules for each Interaction
    - Add ‘food’ Molecules
    - Remove ‘leakage’ outflow Molecules
    - Increment Time

Compound Interactions/1

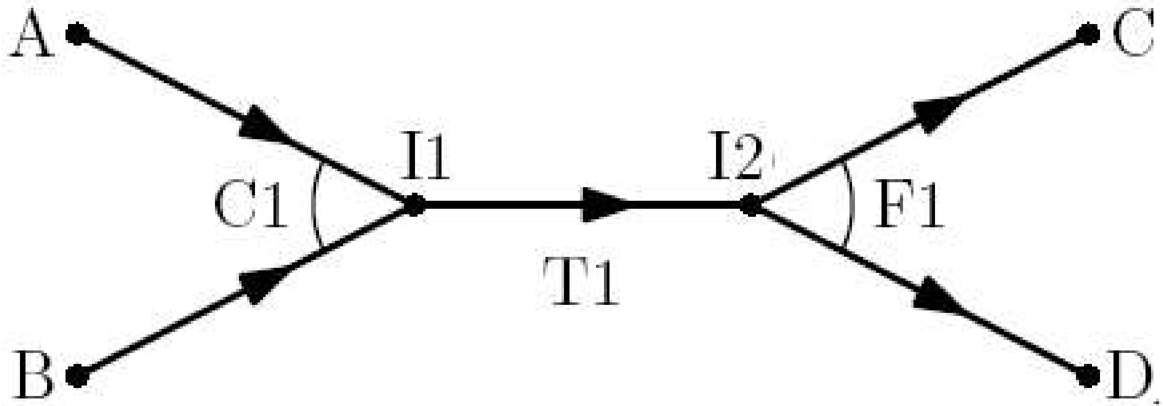
- Why does SimSoup have only three Interaction Types?
- What about more complex interactions?

  $A + B \rightarrow C + D$

  $A + B \rightarrow C$ (with X as a catalyst)

- These more complex interactions cannot be modelled with simple rate laws. They occur in a series of elementary reactions
- The rate of an elementary reaction depends on its molecularity (number of particles coming together)
  - Unimolecular reaction: First Order rate law
  - Bimolecular reaction: Second order rate law
  - Trimolecular and higher: Rare so not modelled

Compound Interactions/2



- A simple network of three Interaction Types

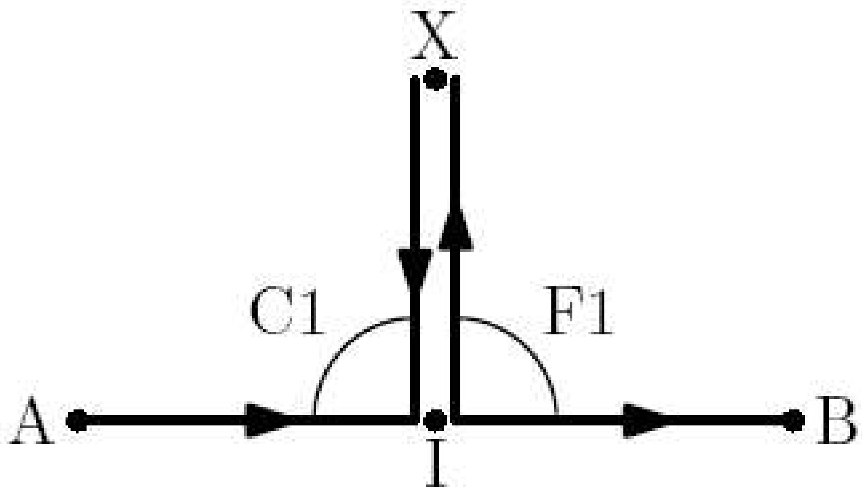
A + B → I1	Construction C1
I1 → I2	Transformation T1
I2 → C + D	Fission F1

- Models a reaction with 3 elementary reactions and scheme

  A + B → C + D

- Overall rate cannot be modelled without taking account of intermediates. These may be taking part in other interactions, so that the behaviour of the system cannot be determined just from the concentrations of A and B

Catalysis in SimSoup/1



- A Combination of two Interaction Types

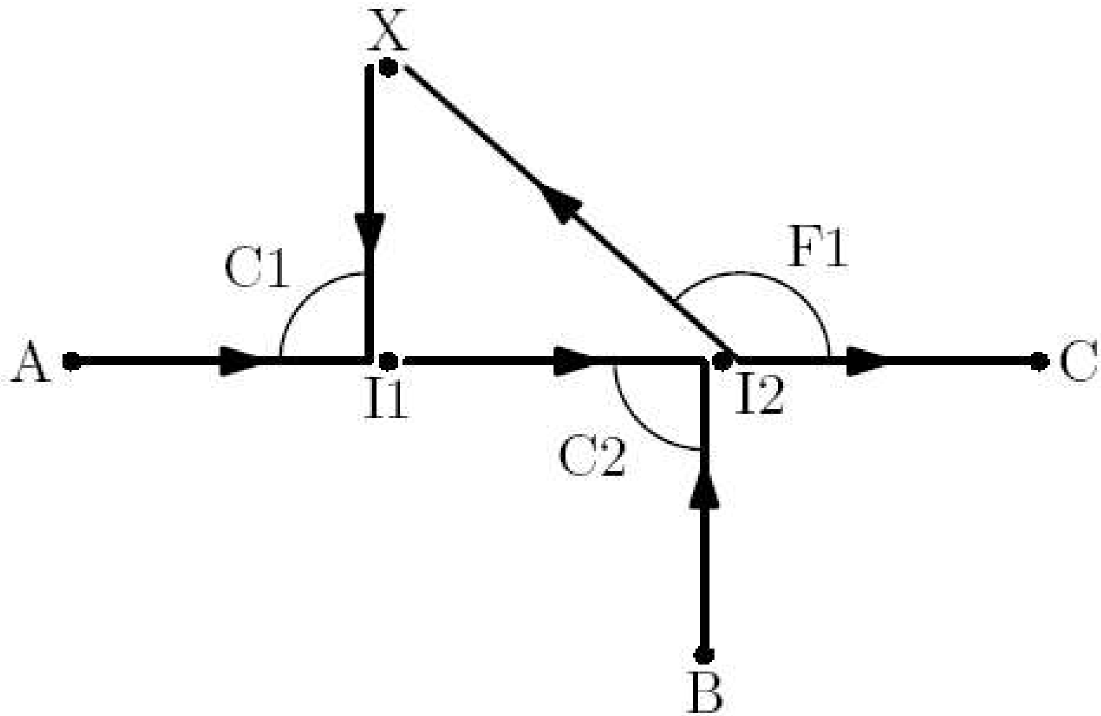
  A + X → I   Construction C1

  I → B + X   Fission F1

- Catalytic Transformation - Overall scheme

  A + X → B + X (X is catalyst)

Catalysis in SimSoup/2



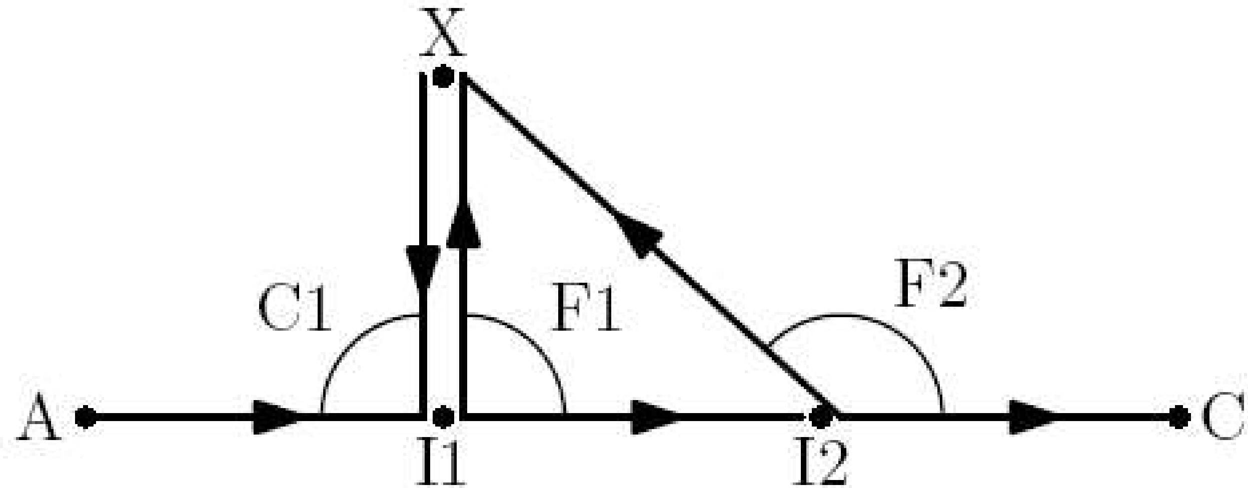
- A Combination of three Interaction Types:-

A + X → I1	Construction C1
I1 + B → I2	Construction C2
I2 → C + X	Fission F1

- Catalytic Construction - Overall scheme

A + B + X → C + X (X is catalyst)

Inheritance: A Compound Interaction that Remembers

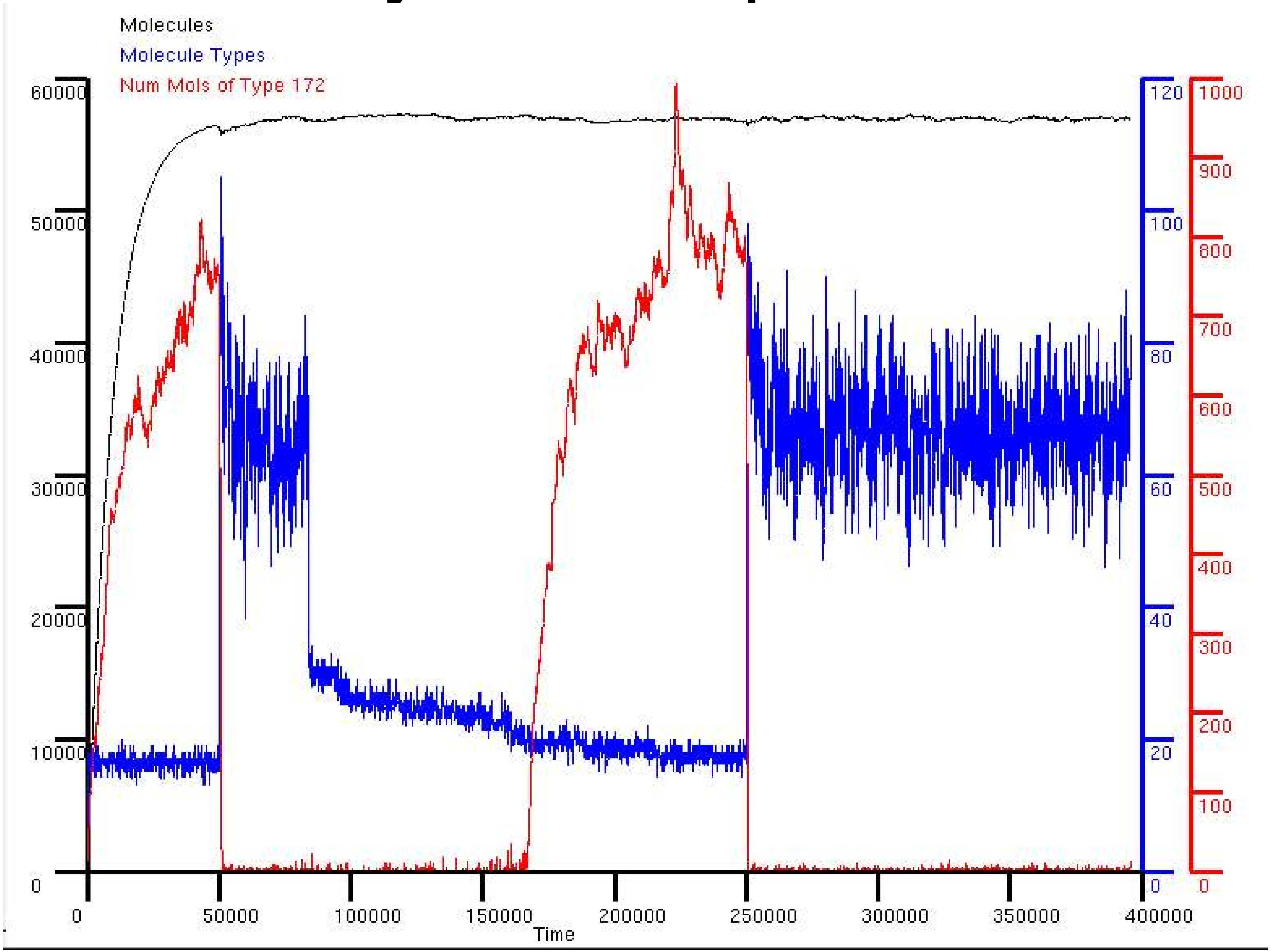


- Overall scheme A + X → C + 2X
- If X is not present, then the reaction does not proceed
- If a single Molecule of type X becomes available, then the reaction begins and continues so long there is a supply of A
- If the Compound Interaction forms part of the metabolic network of a protocell, and A is ‘food’ supply, then the chance introduction of X initiates a new behaviour (production of C). This behaviour is self maintaining and will be passed on to offspring if the protocell divides
- This is non-genetic inheritance.

Preliminary SimSoup Scenario/1

- 200 Molecule Types
- Interaction Types chosen to promote catalysis: 339 Catalytic Transformations
- Start with empty Reactor
- Food supply: One Molecule of each of three types added each timestep
- Cap on growth: Removal probability of 0.0001 for each Molecule at each timestep
- Add 20 Molecules of random types at times 50,000 and 250,000
- Reactor Volume = 1000

Preliminary SimSoup Scenario/2



Preliminary SimSoup Scenario/3

- Interpretation
  - **The network has multiple states that can persist over long periods**
  - **Perturbations can trigger new persistent states:** Eg the perturbations at time 50,000 and 250,000 trigger new high metabolic rate behaviour
  - **High metabolic rate states can be metastable:** Eg **c**atastrophic fallback occurs at about time 80,000
  - **The network remembers what it has discovered:** The persistence of new high metabolic rate states in the face of constant leakage can be regarded as a kind of memory
  - **Fallback of metastable sub-networks:** The rise of Molecule Type 172 at time 170,000 may reflect the fallback of a part of the network (starting just after time 150,000) that was consuming this Molecule Type

Preliminary SimSoup Scenario/3

- Key Issue
  - How many alternative states does the system have?
  - If the number is large, then the ability of the system to enter and remember new states could form the basis for a process of evolution.

Conclusions and Prospects/1

- Conclusions
  - **Simulation can be used to model chemical networks:** It can reflect the full structure of the network and all reaction participants (substrate, catalysts, intermediate products, final products). It allows categories of behaviour to be represented that would be difficult to model using mathematical techniques
  - **Three (elementary) Interaction Types are sufficient:** Eg Catalysis can be represented using Compound Interactions
  - **SimSoup networks have some of the properties needed for evolution:** They can discover and remember new patterns of behaviour. Further investigation is needed, especially in regard to the number and stability of network states.

Conclusions and Prospects/2

- Prospects
  - **Use of SimSoup to invesigate network properties:** Eg by measuring Hamming distance between network states at different times
  - **Open ended growth of network:** Eg an Interaction between Molecules of types that had never previously come into contact would result in the creation of a new Construction and a new Product Molecule Type
  - **Add structure and function to Molecules:** Eg simple structure dependent rules for binding / splitting of Molecules. This would increase the possibilities for evolution.

Thank You