Chemical Evolution of Complex Metabolic Systems

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Abstract
Investigations were undertaken in which a novel computational chemical model system was created to demonstrate the merging of simple cycles to form complex metabolic systems under several sets of conditions. The model described mimicked prebiotic conditions that were present on early Earth when this evolution would have occurred. The model displays a steady state over time when simple systems are merged to form complex systems. Using a very powerful computational program and mathematical analysis, the rate constants and concentration limits were determined that would achieve a steady state for multiple system cases. These results were demonstrated in both the mathematical analysis and the computational output. This computational model of the evolution of complex metabolic cycles suggests a signature for the evolution of life on Earth and elsewhere. A more in-depth understanding allows us to make connections to other theories of origins of life.

Introduction

The origin of life on Earth remains an outstanding topic in science, and the evolution of complex metabolic systems could potentially give insight into this unresolved mystery (1). Many metabolic life cycles are extremely complex and critical to all life on Earth. Examples of these critical metabolic cycles are the Calvin cycle exhibited in photosynthesis and the citric acid cycle that occurs during cellular respiration (2). However, these cycles did not originate on Earth in these complex forms. Rather, a simple metabolic system would have had to existed previously in other environments and later evolved with other simple cycles to their present complexity. In early prebiotic conditions, these simple metabolic cycles could very well have been autocatalytic, meaning that the reaction produces the reactants needed for the ensuing reactions to occur, thus feeding itself without any influence from outside factors.

In order to investigate how complex metabolic cycles evolved, prebiotic conditions must be taken into account (3). One particular topic that has sparked much debate regarding the origin of life is whether or not genes or metabolic cycles came first (4). Geneticists believe that either RNA or an RNA precursor existed first and led to the formation and evolution of metabolic cycles, thus contributing to their complexity. Contrarily, metabolists believe that autocatalytic cycles existed first and over time reactions became more and more complex, therefore causing the formation of metabolic cycles. This research supports the theory stated by Andy Pross (5). According to Pross, it does not matter which came first; rather, the origins of metabolic cycles did not compete with nor inhibit genetic cycles and their evolution. However, the perplexing question must then be asked: how did complex metabolic cycles evolve from simple systems?

Since the metabolic network of life cycles on Earth is extremely complex, it would be fair to assume that the evolution of these cycles from simple systems is a key component to how life originated on Earth. These simple systems can be modeled by the Lotka-Volterra model (6). This model is a set of differential equations derived independently by Alfred Lotka and Vito Volterra to simulate predator-prey interactions. This model shows that as the concentration of prey increases, the concentration of predators will increase due to the increased availability of prey to eat. This will eventually cause the concentration of prey to peak and then decline, because the prey is being eaten up by the predators. Shortly after the prey concentration peak, the predator population will decrease, since there is less prey available for the predators to eat. Since the concentration of the predators is decreasing, this will cause the concentration of the prey to again increase and the cycle will repeat again. This will result in a steady, oscillating cycle of predator-prey concentrations. It is therefore reasonable to ask if these simple cycles could be merged to create a complex metabolic cycle.

Many research projects have focused on the evolution of complex metabolic cycles. Although there are many noteworthy models and experiments, it is important to note that the model developed here is novel and unlike any other model previously explored. This model simulates the classic Lotka-Volterra predator-prey model, as well as the merging of multiple predator-prey models to produce a complex chemical system. Extensive investigations into the model were performed to understand the particular conditions and kinetic characteristics of the model; each of these investigations was performed for each case, particularly for the n=3 case. The models were tested using deterministic computer-based methods as well as mathematical analysis.

Methods

The models were developed and investigated using a kinetics program called Kintecus (7). Kintecus, version 4.01, is a powerful program based on

deterministic methods – the Arrhenius equations – and uses Microsoft Office Excel as an interface. The output from Kintecus underwent mathematical analysis and verification of the output displayed by Kintecus. This program has been used in previous research. The Kinetic initial concentrations for the species in the model are shown in Figures 1 and 2, where A represents the food available for the prey to feed on, X is the concentration of the prey, and Y is the concentration of the predators. The models and the model descriptions for the n=1 case and the n=3 cases are shown in Figures 3 and 4.

Results and Discussion

A chemical model system was designed that simulated the predator-prey relationships of the Lotka-Volterra model (n=1 case). In this model, as the prey population increases the predator population increases due to the increase in availability of food. Eventually, the predators eat too much of the prey and the population of prey declines. This results in the predator population reaching its peak and then declining. This allows the prey population to recover and steadily increase, and thus the cycle is repeated. This resulting oscillating cycle is consistent with the Lotka-Volterra differential equations. After investigating the simple system model, a novel chemical system in which multiple simple systems were merged to form a complex metabolic system was also designed. Three simple cycles were merged together to form a stable metabolic cycle under prebiotic conditions to form the n=3 case. The chemical system was input as a set of chemical reactions into Kintecus and mathematically verified using differential equations. The parameters that were used for Kintecus mimicked prebiotic conditions. See Figures 1 and 2 for the model schemes used for the n=1 case and n=3 case.

Species	Initial Conc.
X	4.00E+00
Y	1.00E+00
A	2.00E+00

Figure 1: Initial Conditions of the n=1 Case. This table shows the intitial concentrations of the classic Lotka-Volterra model, where A is representative of the food available in the system for the prey, X represents the concentration of the prey population, and Y represents the concentration of the predator poulation present in the system.

Species	Initial Conc.
X1	1.00E-01
Y1	1.00E+00
A1	2.90E+00
X2	1.00E-02
Y2	9.90E-01
A2	2.00E+00
X3	9.90E-01
Y3	2.00E+00
A3	1.00E+00

Figure 2: Initial Concentrations for the n=3 Case. This table shows the initial conditions for the model in which three classic Lotka-Volterra autocatalytic cycles were merged. Here again, A is representative of the food available in the system for the prey, X represents the concentration of the prey population, and Y represents the concentration of the predator population present in the system. Each simple cycle contained a food supply, prey, and predators that fed into the next simple cycle.

The model is initially highly variable within limits and oscillates to a steady state. Using the derived mathematical equations, we were able to determine the constants at which the system would go to a stable metabolic state. These differential equations required that the concentrations added up to one to maintain a stable state throughout the cycle. They also verified the results given by Kintecus that showed that a stable state could be obtained when merging the simple cycles. Complex metabolic cycles were mathematically investigated up to the n=14 case and were also consistent with the initially chaotic cycle achieving a stable state. This further verified that simple cycles could successfully be merged to form complex metabolic cycles that achieve a steady state. See Figures 3 and 4 for the Kintecus output that was obtained for the n=1 case and the n=3 case.

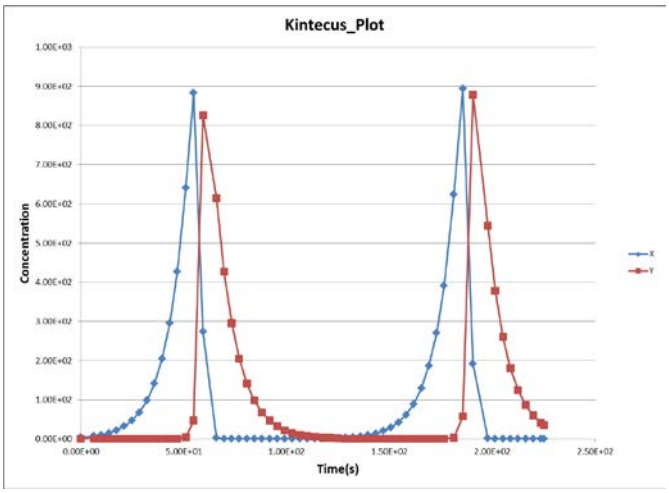

Figure 3: The output for the classic Lotka-Volterra model. The model was run at 300K and exhibited a continous, oscillating steady state.

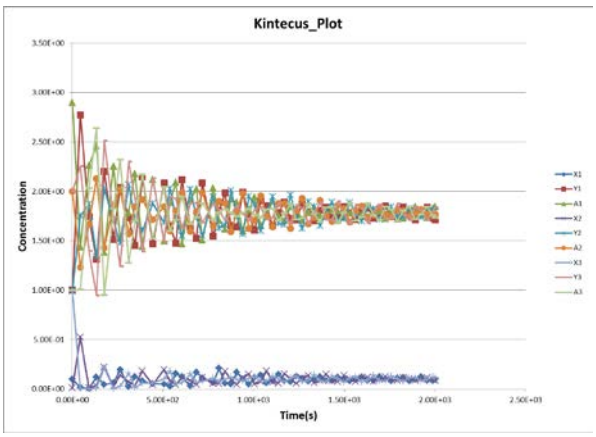

Figure 4: The output for the merging of three simple metabolic cycles (the n=3 case). This model was also run at temperature=300K and achieved a stable state over time.

Conclusions

The origin of life remains a perplexing question and therefore many experiments have been performed to investigate what could have led to these origins. As a result, most of the investigations involve prebiotic chemistry. We are approaching the problem of how complex metabolic systems evolved from a different perspective than that taken by the majority of other researchers.

From the model that was developed, we can suggest that complex metabolic cycles are the result of the merging of simple cycles. We can also infer that a novel model was successfully developed to simulate the outcome of the merging of these simple cycles. From the results displayed by the model output as well as the mathematical analysis, it can also be suggested that the precursor to metabolic cycles was an autocatalytic cycle (8).

Our model is consistent with the theory that the emergence of complex metabolic cycles evolved through the merging of much simpler cycles, which were present on prebiotic Earth. We hope that a more complete understanding of our model will encourage experimental systems that will provide clues to the prebiotic chemistry, which links the evolution of metabolic cycles to present day cycles that are vital to all life forms on Earth. We will continue this research by investigating one cycle in particular: the citric acid cycle (shown in Figure 5) and equating its components to the species present in our model (see Figure 6). As shown in these figures, many similarities can be seen between the citric acid cycle and our novel chemical model developed for the n=3 case. By chemically linking this cycle to our models, we would be able to show that the merging of prebiotic cycles was fundamental in the evolution of complex cycles and thus a key component to the emergence of life on Earth**.**

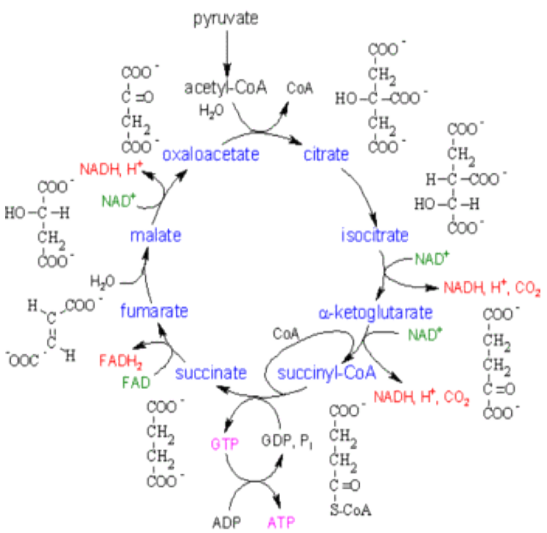

Figure 5: The citric acid cycle

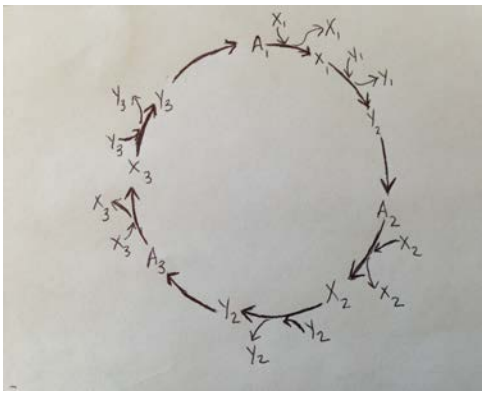

Figure 6: The visual representation of the n=3 complex cycle where A is representitive of the food available in the system for the prey, X represents the concentration of the prey population, and Y represents the concentration of the predator poulation present in the system. As shown above, each simple cycle contained a food supply, prey, and predators that fed into the next simple cycle.

We hope to further investigate our model and develop a more complete understanding of our chemical systems. This will hopefully encourage experimental systems that will provide clues to prebiotic chemistry resulting in simple cycles evolving into complex metabolic cycles on the early Earth.

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Biography

Jackie Kubala is a senior majoring in Forensic Science, Biology Premedical, and Biotechnology and this is her third time doing SURF. She plans on following a path that results in a career in drug discovery and development in a pharmaceutical lab. She is a peer tutor in the Forensics LLC and is an Organic Chemistry teaching assistant. She has been doing research since summer of her freshman year in the chemistry department at UNH. This research will be the focus of her honors thesis. Jackie considers research to be the most rewarding experience she has had at UNH. Jackie is a member of the Forensic Science and Chemistry Club, Honors Student Council, Art from the Heart, Students Making an Impact on their Learning Environment (SMILE), and the Political Science Club. In her free time, she enjoys reading and playing basketball.