

The Good Symbiont

Chrisantha Fernando

Dept. of Informatics, Center for Computational Neuroscience and Robotics,
University of Sussex, Falmer, Brighton, UK, BN1 9RH
ctf20@sussex.ac.uk
<http://www.chrisantha.com>

Abstract. A self-reproducing cycle has the fundamental organization, $A + X \longrightarrow 2A$, and is autocatalytic, i.e. the products catalyze the formation of the products. The rate of increase of A is proportional to A, i.e. exponential. Asexual living entities often grow exponentially when resources are abundant, and decay exponentially when resources are scarce, according to autocatalytic kinetics. If two previously independently replicating autocatalytic entities can form a physical union that is still capable of autocatalysis but with a reduced decay rate, then the symbiosis can be viable in an environment in which resources have been depleted, even if the symbiont has a lower growth rate than either of its component particles. A good symbiont possesses the following features: i. low steric hindrance between components, ii. policing of defection or cheating by symbiont components. iii. low decay rate back to components. iv. absence of emergence of active sites susceptible to decay reactions. v. high rate of the final reproductive step. Failure to form stable symbiosis can result from deficits in any of these features, and is a problem central to the origin of both metabolism and template replication.

1 Recycling Autocatalytic Systems

For persistence of the biosphere, the net ‘biosphere metabolism’ must be recycling [22]. Cells are autocatalytic systems, i.e. fluid automata composed of coupled autocatalytic cycles, at a stoichiometric level, that underly enzymatic catalysis [5]. Therefore we must explain how recycling autocatalytic systems evolved. This paper develops the work of G.A.M King on symbiosis of autocatalysts [1][2][3], by isolating 5 properties that a successful chemical symbiotic event requires.

Autocatalytic cycles must not be confused with ‘autocatalytic sets’, or ‘reflexively autocatalytic systems’, capable of ‘collective autocatalysis’ [7] [8], nor with other models of higher-order replicators [10][9][11]. Autocatalytic cycles consist of stoichiometrically described entities, consisting of small intermediates. Chemically feasible autocatalytic cycles of chemicals exist, for example, the Formose cycle [12], a primitive form of reductive citric acid cycle [14], and the reductive citric acid cycle [15], but only the formose cycle ‘bioid’ has been implemented [13]. No reflexively autocatalytic system is known to exist unless superimposed

upon an autocatalytic cycle. Even recent models of Kaufmann type autocatalytic sets ignore the problem of depleting side-reactions [16], which would turn otherwise neat autocatalytic sets into tar [17]. This problem must be faced head on when tackling autocatalytic cycles [18] [19]. 'Chemical' symbiosis has been explored recently by Fontana and Buss who describe a 'parasite route' to organization, where parasite 'autocatalytic cycles' incompletely deplete a core cycle. However, the likelihood of such a mechanism cannot be addressed with λ -calculus alone[20]. The aim here is not to contribute to the very sophisticated work on symbiosis [21], but merely to confirm that symbiosis of autocatalytic cycles is what needs to be explained.

Consider the simple recycling system containing an autocatalytic replicator in the top right of figure 1. A is the growing state and XA is the reproducing state of the autocatalyst. This translates into the differential equations below.

$$X'(t) = -k_1 A(t)X(t) + k'_1 XA(t) + r_1 DA(t) \quad (1)$$

$$A'(t) = -k_1 A(t)X(t) + k'_1 XA(t) + 2k_2 XA(t) - 2k'_2 A(t)^2 - d_1 A(t) \quad (2)$$

$$XA'(t) = k_1 A(t)X(t) - k'_1 XA(t) - k_2 XA(t) + k'_2 A(t)^2 \quad (3)$$

$$DA'(t) = d_1 A(t) - r_1 DA(t) \quad (4)$$

Figure 1 top left, shows that a stable equilibrium is reached in a recycling system. If the rate of recycling, r_1 , is increased then the constituents of the cycle persist at a higher concentration. There is a fixed point at

$$DA = d_1 A / r_1 \quad (5)$$

$$X = (d_1 k'_1 + d_1 k_2 + k'_1 k'_2 A) / k_1 k_2 \quad (6)$$

$$XA = (A(d_1 + k'_2 A)) / k_2 \quad (7)$$

When $[A] = 0$, $[X_{threshold}] = d_1 k'_1 / k_1 k_2 + d_1 / k_1$. This means that to maintain a non-zero concentration of A , $[X]$ must be greater than $[X_{threshold}]$. The threshold is increased as decay of A increases, and is decreased with increasing forward rates of reaction. Note that the rate of recycling of D into X , r , has no effect on $[X_{threshold}]$.

Figure 1 bottom left, shows another system with the same organization as above, but with a 10 times slower rate of uptake of reagent, Y , and a 10 times slower decay rate. Even though A grows more rapidly than B , at equilibrium a higher concentration of B is maintained at the same rate of recycling.

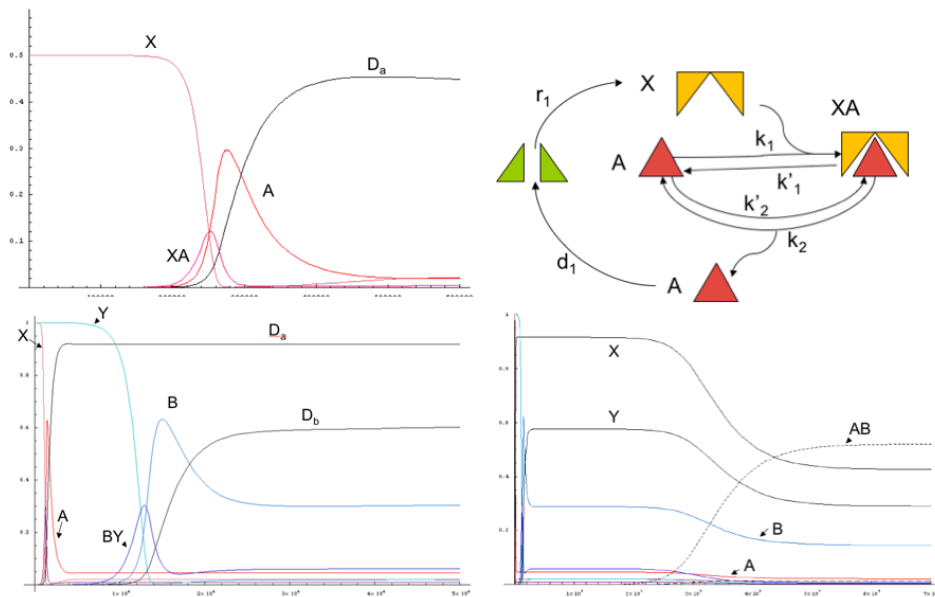


Fig. 1. Top Left: Concentration on the y-axis, and time on the x-axis. $k_1 = 0.001, k'_1 = 10^{-8}, k_2 = 0.0001, k'_2 = 10^{-7}, d = 2 \times 10^{-5}, r = 10^{-6}$. Initial $[X] = 0.5M$, Initial $[A] = 10^{-7}M$, and all other concentrations = 0. $[X]$ decays, being converted into A and XA , and eventually decaying to D , which is recycled by some environmental process, e.g using light energy, back into X . After an initial overgrowth of A , equilibrium is reached. **Top Right:** A simple recycling autocatalytic system. A uses the food molecule X forming the intermediate XA . A catalyses a conformational change in X to produce another A molecule. Therefore 2 A molecules pass out of the reaction. A degrades to D , and D is recycled by some environmental process, e.g using light energy, back into X . **Bottom Left:** Concentration on the y-axis, and time on the x-axis. For the autocatalytic particle B , the reaction network is of identical topology to particle A . $k_2 = 0.0001, k'_2 = 10^{-8}, k_3 = 0.00001, k'_3 = 10^{-8}, d_2 = 2 \times 10^{-6}, r_2 = 10^{-6}$. Initial $[Y] = 0.5M$, initial $[B] = 10^{-7}M$. The concentrations of particle A and its products are included for comparison. Note particle A grows faster and earlier than particle B , but that particle B reaches a higher equilibrium concentration than A . **Bottom Right :** y-axis: Concentration, x-axis: Time. Note the long timescale compared to figures 2 and 3. A and B increase to reach their previous equilibrium concentrations. However, the particle AB (small dashed line) invades the population to eventually reach a higher concentration than A and B . YAB (large dashed line) exists at lower concentration, and $XYAB$ at even lower concentration (not visible).

2 Symbiosis of recycling autocatalytic particles

Now imagine that the two particles A and B can very rarely join together in the reaction $A + B \rightarrow AB$, with a forward rate of as and a backward rate $as'{}^1$.

¹ King has elsewhere considered the symbiotic event to be the association not of A and B , but of XA and YB . Also he has compared the symbiotic state not with two

Assume that the system starts with a very small amount of AB (the symbiotic particle), i.e. 10^{-9}M , in the presence of a much larger amount of A (0.0001M), and B (0.0001M). For the moment let us prevent the formation of further AB by association between A and B , but still allow degradation of AB into A and B at a low rate, $as = 10^{-7}\text{sec}^{-1}$. This simple autocatalytic system is shown in figure 2 and described by the equations below.

$$\begin{aligned} X'(t) = & -k_1A(t)X(t) + k'_1XA(t) + r_1DA(t) + j'_1XYAB(t) \\ & - j_1YAB(t)X(t) \end{aligned} \quad (8)$$

$$\begin{aligned} A'(t) = & -k_1A(t)X(t) + k'_1XA(t) + 2k_2XA(t) - 2k'_2A(t)^2 - d_1A(t) \\ & + as'AB(t) - asA(t)B(t) + j_2XAB(t) + d_5XYAB(t) \end{aligned} \quad (9)$$

$$XA'(t) = k_1A(t)X(t) - k'_1XA(t) - k_2XA(t) + k'_2A(t)^2 \quad (10)$$

$$DA'(t) = d_1A(t) - rDA(t) \quad (11)$$

$$\begin{aligned} Y'(t) = & -k_3B(t)Y(t) + k'_3YB(t) + r_2DB(t) - j_3Y(t)AB(t) \\ & + j'_3YAB(t) \end{aligned} \quad (12)$$

$$\begin{aligned} B'(t) = & -k_3B(t)Y(t) + k'_3YB(t) + 2k_4YB(t) - 2k'_4B(t)^2 - d_2B(t) \\ & + as'AB(t) - asA(t)B(t) + d_3YAB(t) + d_4XYAB(t) \end{aligned} \quad (13)$$

$$YB'(t) = k_3B(t)Y(t) - k'_3YB(t) - k_4YB(t) + k'_4B(t)^2 \quad (14)$$

$$DB'(t) = d_2B(t) - r_2DB(t) \quad (15)$$

$$\begin{aligned} AB'(t) = & asA(t)B(t) - as'AB(t) - j_3Y(t)AB(t) + j'_3YAB(t) \\ & - 2j'_0AB(t)^2 + 2j_0XYAB(t) + d_3YAB(t) + j_2XAB(t) \end{aligned} \quad (16)$$

$$\begin{aligned} YAB'(t) = & j_3Y(t)AB(t) - j'_3YAB(t) + j'_1XYAB(t) - d_3YAB(t) \\ & + d_5XYAB(t) - j_1YAB(t)X(t) \end{aligned} \quad (17)$$

$$\begin{aligned} XYAB'(t) = & -j_0XYAB(t) + j'_0AB(t)^2 - j'_1XYAB + j_1YAB(t)X(t) \\ & - d_4XYAB(t) - d_5XYAB(t) \end{aligned} \quad (18)$$

$$XAB'(t) = d_4XYAB(t) - j_2XAB(t) \quad (19)$$

If the reactions shown in Figure 2 can take place, AB will be autocatalytic. Imagine that in the particle AB , the subunit A_{ab} does not block the active site of the subunit B_{ab} for Y , and so let Y react with B_{ab} to produce YAB at the same rate $j_3 = k_3$, as B associates with Y to produce YB . Assume also that Y can dissociate from YAB at the same rate as Y dissociates from B (i.e. $j'_3 = k'_3$). Assume that the subunit YB_{ab} on YAB has the same properties as YB , so that dissociation of YAB into $AB + B$ occurs at the same rate (i.e. $d_3 = k_4$) as

previously independently replicating chemical species but with two species previously associated by mutual exchange of materials, i.e. the products of A are the food molecules of B and vice versa. The intermediate stage is not necessary (logically) for the emergence of physical union, although it may have promoted spatial associations between particles that would otherwise have not existed [3].

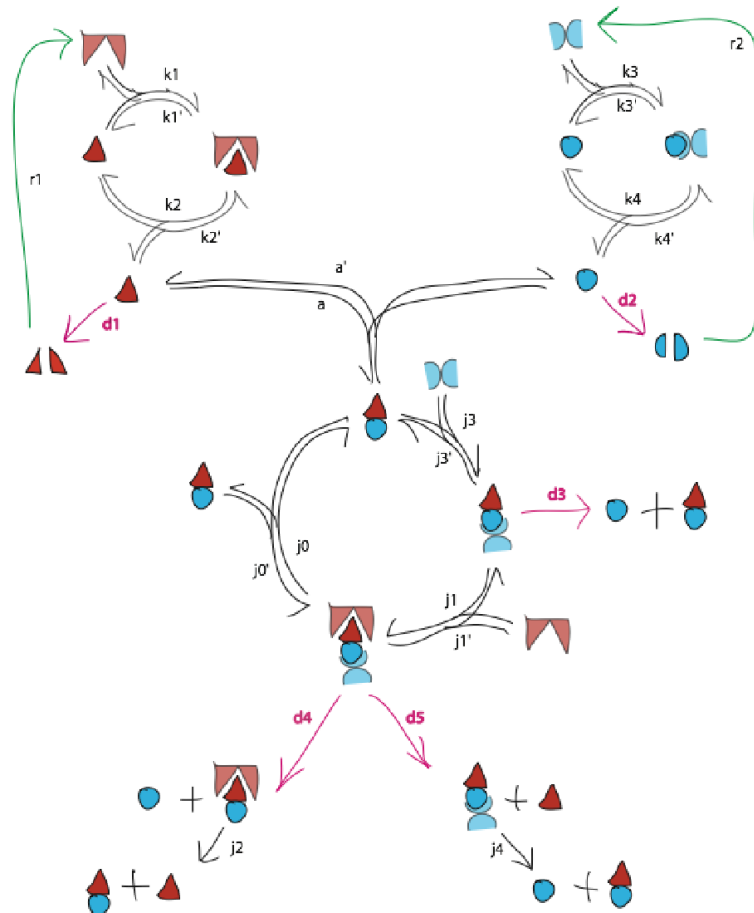


Fig. 2. Shows the higher order autocatalytic cycle of AB , the independent cycles of A and B , and the corresponding decay reactions. A is the red triangle, B is the blue circle. X is a pale red double triangle shape, and Y is the pale blue pair of hemi-circles. Complexes are shown as combinations of these elements. Rate constants correspond to those described by eqn. 8 to 19.

dissociation of YA to produce $2B$. This is a tapping side-reaction of the autocatalytic cycle of AB . The reverse reaction $AB + B \rightarrow YAB$ is ignored, as

it can only help the replication of AB . Assuming that YB_{ab} does not interfere with A_{ab} 's active site for X , then X can associate with YAB to form $XYAB$ at the same rate as A associates with X independently (i.e. $j_1 = k_1$). The same is true for the reverse reaction (i.e. $j'_1 = k'_1$). Assume that $XYAB$ is subject to two possible side-reactions. Let it decay to $B + XAB$ at rate $d_4 = k_4$, and into $A + YAB$ at rate $d_5 = k_2$, again assuming no steric interference between the active sites of subunits XA_{ab} and YB_{ab} . XAB then reacts to form AB and A at rate $j_2 = k_2$. The formation of XAB by AB binding to X , before Y binds to AB , has been ignored. This would either produce another possible autocatalytic cycle with X binding first and Y binding second, or produce a non-cycling decay chain. The consequences of this alternative cycle are significant but here it is assumed that XAB cannot re-enter the cycle apart from by further decay into food molecules. $XYAB$ can complete the autocatalytic cycle by promoting the simultaneous uni-molecular conformational change of $XYAB$ into $AB + AB$. It is assumed that this occurs at the forward rate of $jz = 0.001 = k_2 > k_4$, although it may be more reasonable to expect that it would take the sum of the average period of dissociation of A from XA and B from YB , i.e. $(k_1^{-1} + k_2^{-1})^{-1}$.

Figure 1 bottom right, shows the concentrations of substrates for the reaction system described above. Each species undergoes exponential growth followed by depletion. Growth of the symbiont is delayed not because it must be produced by further symbiosis (these are forbidden), but because of its initial low concentration and lower growth rate than A or B . Its growth is limited by the X and Y concentrations that have been established previously by the growth of A and B . Nevertheless eventually AB outgrows A and B , and A and B continue to persist at low concentrations.

3 Kinetic Analysis

How do the kinetic properties of the particle AB affect the equilibrium concentration of AB ? The system behaviour in figure 1 bottom right, is dependent on the following assumptions.

1. A_{ab} does not interfere with the binding of Y to B_{ab} , and B_{ab} does not interfere with the binding of X to A_{ab} . This means $j_3 = k_3$, $j_1 = k_1$ and $j'_3 = k'_3$, $j'_1 = k'_1$.

2. A_{ab} does not interfere with the production of B from YAB , nor from $XYAB$. B_{ab} does not interfere with the production of A from $XYAB$. This means that $d_3 = d_4 = k_4$ and $d_5 = j_2 = k_2$.

3. The rate of production of $2AB$ from $XYAB$ is equal to the rate of production of $2A$ from XA . This means $jz = k_2 > k_4$. jz' is negligible.

4. The decay of AB into A and B , (as), occurs at a low rate, 10^{-7} , and the rate of production of AB from A and B , (as), is zero. The results are similar if the rate of production, (as), of AB is 10^{-14} and the initial concentration of AB is 0.

5. AB does not undergo emergent decay reactions caused by novel active sites uncovered by their union. This means no alternative decay reactions of AB other than those above have been considered.

As with any autocatalytic cycle, the concentration of constituents reaches a fixed point when the rate of production of constituents equals the rate of decay of the constituents. The fixed point $[AB^*]$ is determined by the assumptions, which are now relaxed.

3.1 Interference Between Components

Assume that S_{ab} is the steric hindrance of A upon the binding of Y to B , and S_{ba} is the steric hindrance of B upon the binding of X to A . Both range from 0 to 1, 1 being maximal hindrance and 0 being no hindrance. Let $j_3 = (1 - S_{ab})k_3$ and $j_1 = (1 - S_{ba})k_1$. What happens to the equilibrium concentration of AB as S_{ab} and S_{ba} are varied? Figure 3 top left, shows the equilibrium concentration of AB for different values of S_{ab} and S_{ba} . At high values of steric hindrance $[AB^*]$ is virtually zero.

3.2 Policing by Components

Assume that A_{ab} is actually able to prevent the premature detachment of Y from YAB to produce B , and also of Y from $XYAB$, by an equal amount. Therefore let $d_3 = d_4 = k(1 - P_{ab})$ where P_{ab} is the extent of protection or policing afforded by A_{ab} to Y . Also let B_{ab} protect the X particle from premature detachment from XAB and $XYAB$, so that $d_5 = j_2 = k_2(1 - P_{ba})$. Assume that S_{ab} and S_{ba} are reset to 0 as before.

As expected figure 3 top right, shows that $[AB^*]$ increases with increasing policing by A_{ab} of B_{ab} and B_{ab} of A_{ba} . However, at very high values of P_{ba} the cycle is drained into XAB which cannot decay. This anomaly is due to our assumption that XAB can only take part in one decay reaction. Note the build up of XAB by the irreversible reaction at rate d_4 , but since $P_{ba} = 1$ then $j_2 = 0$ so XAB builds up.

3.3 Reversion to Components, and Reproduction Rate

Let us reduce the rate of the reproduction reaction producing $2AB$ from $XYAB$. Let $jz = Rk_2$ where R ranges from 0 to 1. Also let us make $as' = 10^{-7}F$,

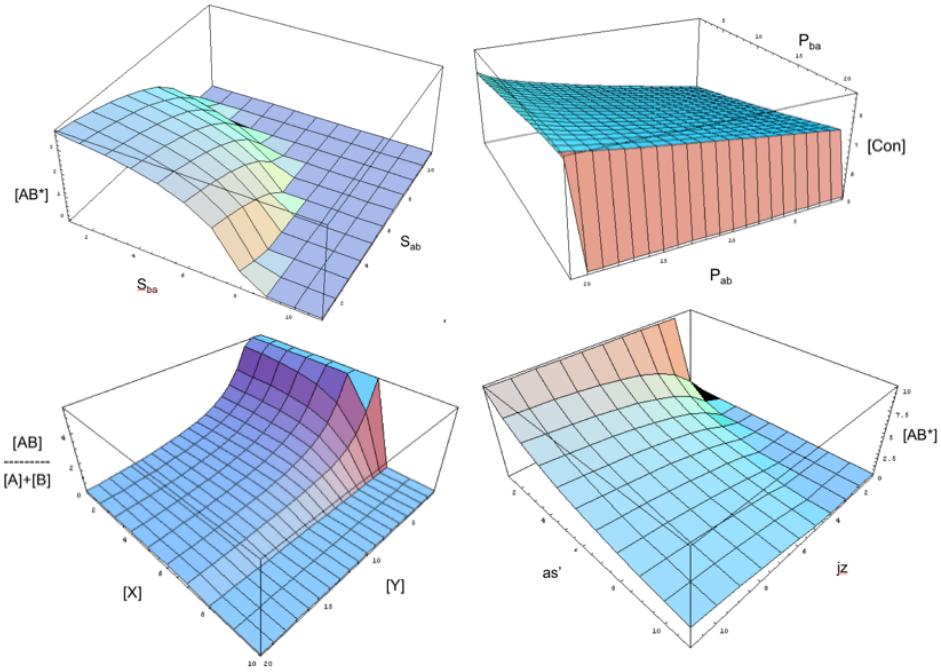


Fig. 3. Top Left: Steric Hindrance between components can prevent symbiont replication. $[AB^*]$ drops off rapidly at high rates of hindrance resulting in very low concentrations of AB . **Top Right:** The z-axis shows not $[AB^*]$ alone, but the summed equilibrium concentration of all configurations of AB , i.e. YAB , $XYAB$, AB , and XAB . The symbiont has greater concentration with greater amounts of protection of premature detachment. There is an anomaly at high P_{ba} , where $[AB^*]$ actually decreases rapidly. This is associated with an increase in $[Y]$ and $[XAB]$ and a decrease in $[YAB]$, $[AB]$ and $[XYAB]$ and is explained because the cycle is tapped by XAB which cannot be recycled with maximal policing of A by B . **Bottom Left:** The z-axis shows the ratio of AB particles to A and B particles. At low $[X]$ and low $[Y]$, AB dominates, but increasing either one makes the simpler particles more successful. The sensitivity of $[AB^*]$ to increasing $[X]$ is sharper than its sensitivity to increasing $[Y]$. **Bottom Right :** jz was increased from 0 to k_4 in 100 increments. There is a threshold of jz below which $[AB^*]$ is very low. This threshold depends on as' . as' was increased from 0 to 10^{-7} and as expected $[AS^*]$ decreased as decay of AB into A and B increased.

where F ranges from 0 to 1. Reset S_{ab} , S_{ba} , P_{ab} and P_{ba} to 0. Figure 3 bottom right, shows the results we expect, that decreasing as' increases $[AB^*]$, as does increasing jz . Note that below a threshold of jz , $[AB^*]$ decreases rapidly to zero.

3.4 The Effect of Resource Concentration.

AB competes for the same reactants as A and B . All follow the overall growth law shown below, where C is the constituent concentration, β the growth rate, α the decay rate, and R the resource concentration, $dC/dt = -\alpha + \beta R$. When R is high, growth is dominated by β , but when R is low, decay (the α term) predominates. The growth of the fastest constituent (A in this case) depletes R , and starts the process of decay rate based selection, where particles with low α decay more slowly. This simple process is slightly complicated due to the presence of two resources X and Y . Figure 3 bottom left, shows the effect of increasing X from 0 to 0.03M and Y from 0 to 0.02M, and keeping them fixed at these values by magical topping up. Each particle is started at the same initial concentration, 0.0001M. The z-axis shows the ratio $[AB]/([A]+[B])$. It shows that AB obtains higher values relative to A and B , at low resource concentration.

4 Conclusion

If the symbiont can reduce its decay rate relative to the composing particles decay rates, then it can obtain higher equilibrium concentrations. However, at high resource concentration selection is on the basis of growth rate, not decay rate, and here A and B out-compete AB , since growth is exponential, and the growth rates of A and B are greater (under reasonable assumptions) than the growth rate of AB . Once AB depletes X and Y to even lower levels, another autocatalytic particle may arise which utilizes a wider range of food molecules, e.g. $ABCD$, using P and Q as food, if appropriate particle varieties exist. The probability of further symbiosis depends on particle structure. How can the specificity of reactions required for a successful symbiont be achieved? In chemistry this is done by addition reactions that consume active sites. King proposes that the coordination compounds of metal ions in aqueous solution have the appropriate properties.

The problem of reducing the decay rate of the autocatalytic particle is a very general one for the origin of life. It is encountered in the origin of metabolism in the problem of how the autocatalytic formose cycle can be viable (e.g. in the chemoton) when it is subject to so many side-reactions, and where no enzymes are yet available [4][5]. The side-reaction problem is surprisingly also faced in non-enzymatic template replication, in which a chain of coupled autocatalytic cycles of replicating templates are tapped by elongating side reactions. How the side-reaction problem can be solved defines a continuing research program [6].

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