

# Life-Span Expectancy and Cycle Size in the Original Autopoiesis Algorithm

Siddharth Priya<sup>1</sup> and Chrystopher L. Nehaniv<sup>1,2,3</sup>

<sup>1</sup>Dept. of Electrical and Computer Engineering    <sup>2</sup>Dept. of Systems Design Engineering  
University of Waterloo, Waterloo, Ontario, Canada

<sup>3</sup>Royal Society Wolfson Biocomputation Research Laboratory  
University of Hertfordshire, Hatfield, United Kingdom

## Abstract

We implement Varela, Maturana and Uribe's original *autopoiesis* algorithm with suitable modifications as proposed by McMullin. We further investigate how environmental factors affect formation of autopoietic entities - namely how long an entity remains a whole after formation and to what size does it grow in its life span i.e. Life span and Cycle size respectively. We find that ratios of different basic elements like Holes, Substrates and Catalysts do not affect Life span and Cycle size meaningfully but both properties are affected negatively if disintegration probability—the probability of a Link element to transform into a Substrate element—is increased.

## Introduction

Autopoiesis is a profound generalization of homeostasis proposed by Varela, Maturana and Uribe (1974) as the defining feature of life, or at least a necessary feature of life wherever and in whatever media it may exist, on earth or elsewhere in the universe. An autopoietic system is not only self-maintaining, but *self-producing*, maintaining a distinction between itself and its ambient environment. Most fundamentally, it establishes and maintains a 'membrane' or 'boundary' enclosing it and mediating inward and outward fluxes of material and information; moreover, it does this by means of the ongoing activity of a "circular" network of processes that construct its own components, including the machinery for doing so. An autopoietic entity embodies a process of organizational closure and its activity enacts the continuity of this organization. The identity of the living individual is thus such a *process*, that like a wave persists despite change in its material constituents.

Autopoiesis reduces the properties of life to basic concepts like self-organization and self-repair (McMullin, 2004). The earliest computational model of autopoiesis employed simple local, time-invariant rules that made these properties emerge. While the original paper (Varela et al., 1974) illustrates the environment and algorithms in detail<sup>1</sup>,

<sup>1</sup>Algorithmic details have been made more precise in FORTRAN code for the original Autopoiesis algorithm made available by Barry McMullin (1997) and clarified in his papers cited here.

the simulations themselves have not been analysed for the impact of different configuration parameters, e.g., different initial starting configurations; different decay and catalyses rates; nor in conditions supporting more than a single entity. Here we present a new implementation<sup>2</sup>, and analysis of how the simulation performs for such different configuration parameters. Simple automated measures of *life span* and *cycle size* to determine their distributions in different conditions, each with multiple repeated runs in order to gain insight into their dynamics and robustness properties. Larger ambient universes than in the seminal work involve multiple computational autopoietic entities.

## Background: What is Autopoiesis?

Autopoiesis as conceived by Varela and Maturana (1980) is a phenomenon which creates a self-organizing and self-maintaining unity in a dynamic environment. They argue that all life is autopoietic self-evidently and that autopoiesis describes the self-organization of life (Bitbol and Luisi, 2004). Concise criteria<sup>3</sup> for *autopoiesis* are: "(1) that the system builds its own boundaries; (2) that this construction is due to reaction(s) (activity) taking place within the system; (3) that it is performed through reactions determined by the system itself." (F. J. Varela in 2000 as quoted by Bitbol & Luisi (2004).)

Living things as we know them on Earth from prokaryote cells on up through differentiated multicellular organisms, even if they cannot reproduce (including mules or non-fertile humans), all exhibit autopoiesis. Other agents in evolving populations may not be, e.g., a DNA or RNA virus produces neither its own protein coat nor the nucleic acids within its boundary - the living host cell produces these! (Luisi, 2003). Similarly, artificial life agents such as Tierrans (Ray, 1992), evoloops and variants (Sayama, 1999; Oros and Nehaniv,

<sup>2</sup>We have open sourced the object-oriented implementation in Python used in this work in the hope that it will also be useful to the Artificial Life research community: Autopoiesis System <https://github.com/priyasiddharth/autopoiesis-system/>.

<sup>3</sup>These are much simplified in comparison to the six-step key of Varela et al. (1974).

2007), other self-replicators and self-reproducers (von Neumann, 1966; Langton, 1984) are not autopoietic, but ‘fragile’. They do nothing to counter external perturbations, and evidently house no processes that actively maintain their identity, their boundaries, spatial and production closure.

McMullin (2013) more recently characterized autopoiesis in terms of two intertwined organizational system properties: “Closure in *production*: The system is composed of components which give rise to (realize or instantiate) processes of production which, in turn, collectively produce more of those same components” and “Closure in *space*: The self-construction of a boundary between the system and the world in which it is embedded, yet from which it distinguishes itself”.

**Autopoiesis and Reproduction** If the boundary of an autopoietic entity is comprised of bonded link elements  $L$ , denote the rate of disintegration of link elements by  $v_{dec} = d[L]/dt$  and the rate of generation of link elements  $v_{gen} = d[L]/dt$ , where  $[L]$  is the concentration of the chemical species than can link to form a boundary. Depending on whether the net rate of production of these boundary surface components  $v_{gen} - v_{dec}$  is negative, zero, or positive, one can obtain, respectively: death and degeneration, balanced self-maintenance (autopoietic self-maintenance), or growth and reproduction, as has been demonstrated physically in self-replicating micelles by manipulating the chemical medium (Zepik et al., 2001; Luisi, 2003).

Similarly, Jean Sirmay has created an alternative model of computational autopoiesis on hexagonal lattice (Sirmay, 2011) and explored its connections to self-reproduction (Sirmay, 2013). Intuitively, a self-producing, self-maintaining system if split in two with each component able to repair and regenerate its boundary and internal activity exhibits reproduction. Such splitting results in the generation of new entities. This is observable in self-producing micelles which grow until they become unstable and split in two (Bachmann et al., 1990, 1992).

Thus, autopoiesis can be a route to reproduction as an emergent side-effect of autopoietic activity, rather than reproduction being pre-requisite for life and autopoiesis.

**Autopoiesis, Life, Cognition** Maturana and Varela (1980) even went so far as to identify life and cognition with the organizational structure of autopoiesis, a persistent *identity*, the process of producing the producer (Luisi, 2003).

Bitbol and Luisi (2004) refine this with arguments that minimal autopoiesis is necessary for both, but sufficient for neither. They introduce a hierarchy of autopoietic organization ranging from (0) minimal autopoietic systems such as self-producing lipid micelles and vesicles where autopoiesis occurs at the boundary, without the capacity to regulate intake and outflow of nutrients, waste or information signals (Zepik et al., 2001; Szostak et al., 2001; Luisi, 2003), to

those able to assimilate perturbatory change passively (0) or actively (1) while maintaining dynamic structural stability through selective update of nutrients and expulsion of waste in the discriminative use of metabolites, or (2) to accommodate disturbances with architectural re-organization, respectively, or act in ways may suggest to an observer content, representation-like behaviour, and (4) exhibit intersubjective abstraction, predicative rules, knowledge and language (4)+. See (Bitbol and Luisi, 2004) who locate life at minimal cognitive levels (1) or perhaps (2) and above. Level 0, with its null level of cognition, characterizes non-living autopoietic entities such as lipid bilayer micelles whereas bacteria display minimal cognition characteristic of life. All of these levels from the null level of cognition upward are built upon autopoiesis at their core to endowing the system to enact meaning and purpose in achieving its own implicit goal of self-maintenance and self-production through its own activity.

In contrast, others such as Bourguine and Stewart (Bourguine and Stewart, 2004), consider as *cognitive* systems that act through linking ‘inputs’ and ‘outputs’ so to as to promote “viability”, i.e., adaptive sensing and actuation (with not necessary being autopoietic). They, while characterizing *living* systems those in the intersection of the cognitive and the autopoietic remark that ‘viability’ in this sense of cognition might be from the perspective of an external observer, e.g. the builder of the system, or from the perspective of the system itself (if it is an autopoietic entity, then adaptivity and viability are natural defined as its own persistence and continuity as such).

## The Original Minimal Autopoietic Computational Model

Here we return to the roots of the subject with the first article published on the autopoiesis in English (Varela et al., 1974). To make their claims concrete, the authors gave a series of axioms characterizing for autopoiesis, in the form of a six-point key to test whether or not an entity is autopoietic (Varela et al., 1974). They exhibited a simple computational instantiation of a system satisfying these requirements which demonstrates this both self-organizing and self-maintaining behaviour. In our work, we implement another instantiation of the original Varela-Maturana-Urbe model including modifications suggested but not carried out by McMullin (1997) (see below). We go on to investigate its properties under various initial distributions of material and in different sized environments, its robustness to different probabilities of the degeneration of links, and study the life-span of autopoietic entities in the model.

The original computational model implements autopoiesis under the continual probabilistic disintegration of link elements with probability  $P_d$ , while a catalyst promotes the formation of new link elements from substrate particles. These link elements, which are produced and present in

higher concentration near the catalyst (and eventually inside the entity), diffuse and are available to replace links in the oligomeric chain comprising the boundary (a cycle of links bonded to neighbours in the chain). This endows the entire organization with self-maintenance capacity, balancing ruptures due to disintegration of the boundary cycle.

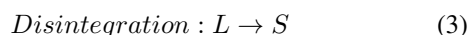
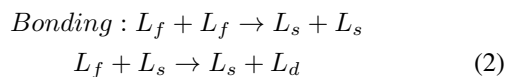
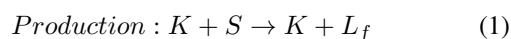
## The Autopoietic Model

**Basic Elements and Reactions** The world consists of a 2-D grid comprised of locations called cells. Each cell can have one of four possible elements.

1. Substrate (S) is a pre-cursor species of the raw material to form the boundary of autopoietic entities.
2. Link elements (L) form may bond with other Link elements. They can be in three states - free ( $L_f$ ), singly bonded ( $L_s$ ) and doubly bonded ( $L_d$ ).
3. Catalyst (K) elements make possible the reaction to convert S elements to L elements.
4. Holes (H) correspond to empty space in the universe. If a cell does not contain any other element, it contains a hole.

In addition, part of the state of world includes, for each link element, which neighbouring link elements are bonded to it (a bonding edge). A link element can be bonded to either zero, one or two of its neighbours.

The following chemical reaction-like processes take place in this world.



Disintegration can happen to all three kinds of link elements.

**Variations of the Original Reactions** Note that reactions (1) and (3) differ from the original formulation of (Varela et al., 1974) which uses two S elements for production and creates two S elements during disintegration. This is done to avoid a non-local operation during disintegration which places an extra S element anywhere in the grid. Such a global search or random displacement over arbitrary distances for placing an S element would be contrary to our purposes of studying global emergence from local interactions.

Indeed, McMullin (1997, p.15) observes that the original formulation creates a potential problem for locality, when two substrate elements S combined to form a single link element L a hole arises locally, but disintegration producing two S elements may result in nowhere to place one of them in the vicinity of this event. Using one instead of two S elements in production balances disintegration producing one

		X		
	N	N	N	
X	N	E	N	X
	N	N	N	
		X		

Figure 1: Arrangement of Neighbours(N) and Extended Neighbours(X) for an Element(E)

S instead of two. This is in line with McMullin's analysis (1997, p.3) that "nothing in the phenomenology of the model would rely on this 2:1 ratio in the composition reaction." He writes "*if the reaction were redefined so that a single S could be transformed to a single L particle (and vice versa for disintegration) then this whole difficulty would disappear anyway*" (McMullin, 1997). Taking this suggestion in italics we implemented this variant of this original autopoietic model with the variant reactions rules (1) and (3) as above.

**Further Details** There are three properties of the original and our model to note.

1. Elements move across the grid with a time step according to local processes governed by *rules*. These rules generally imply that S, L, K, H elements are heaviest to lightest and thus a heavier element can displace the lighter one.  $L_s$  and  $L_d$  are immobile and cannot displace other elements.
2. The production and bonding reactions require coordination amongst two elements and this always takes place between neighbours. Some processes also take extended neighbours into account. See Figure 1 for neighbourhood structure.
3. Apart its location in the grid, each link element  $L$  tracks which, if any, other link elements  $L$  is bonded to. This information together with the matrix of elements then constitute the state of the universe at a given moment.

There are seven distinct processes in the original algorithm that occur between time instants: Note each time instant is here is a 'snap-shot' of the dynamics, with possible movement of elements and breaking and reforming of links between the these instants. Between two time instants the following processes occur in order 1 to 5, with 6 and 7 appropriately interleaved at the end of each (details follow):

Bonding occurs for every step 1 to 4 and Rebonding occurs specifically in the Disintegration step, therefore only steps 1 to 5 are considered as high level processes, 6 and 7 being sub processes. A summary of each process follows.

**1. Motion of Holes** The masses of S, L and K elements are greater than H elements, therefore they can swap places with H at-will. This step swaps each H particle in the grid with one of its immediate or extended neighbours. The extended

neighbour case allows for an S particle to move across a bonded L particle. In the end, step 6 (Bonding) is called.

**2. Motion of free Links** This step considers all  $L_f$  elements in the grid. An  $L_f$  can affect positions of neighbouring S and H elements since L elements have greater mass than either of them. Similarly, it cannot displace a K particle. An  $L_f$  does not move another  $L_f$  presumably since this complicates the algorithm (McMullin, 1997) while an  $L_s$  or  $L_d$  (bonded link) cannot be moved by the rules of the universe. A neighbouring H is simply swapped with the L element, while an S element is displaced using more involved rules which are as follows.

1. If S element has a neighbouring H, exchange S and H and subsequently H and L. *OR*
2. If S element has a neighbouring  $L_s$  or  $L_d$  which in turn contains an H then swap H and S similar to Step1 (Motion of Holes) and then swap H and L.

In the end, step 6 (Bonding) is called.

**3. Motion of Catalysts** This step considers all catalysts in the grid. A catalyst (K) element can move neighbouring L, S and H elements since it has greater mass:

1. An  $L_f$  element can be moved according to rules in Step 3 (Motion of free Links). If this is impossible, then exchange K and  $L_f$ . Note that  $L_s$  or  $L_d$  elements cannot be moved.
2. An S element can be moved according to the rule in Step 1 (Motion of Holes) pertaining to exchanging S and neighbouring H elements.
3. An H element can be exchanged with the K element.

In the end, step 6 (Bonding) is called.

**4. Production** This step considers all Catalysts in the grid. A Catalyst(K) element which has a neighbouring S element can, with probability  $P_p$  produce an  $L_f$  element such that the S is used up and replaced by  $L_f$  *in situ*.<sup>4</sup> In our experiments,  $P_p = 1 - P_d$ . See Step 5 (Disintegration) for details on  $P_d$ . In the end, step 6 (Bonding) is called.

**5. Disintegration** This step considers all Links in the grid. An L element, either free or bonded can choose to spontaneously disintegrate into an S element *in situ* with probability  $P_d$ . Links, if any, with neighbouring L elements are broken. Subsequently, step 7 (Rebonding) takes place at the site (i.e. around the cell under discussion).

<sup>4</sup>Using a parameter for the probability of catalysis (reaction 1) in our variant of the original model implements a suggestion of (McMullin, 1997, p.12) that the rate at which production occurs “could instead be made subject to a reaction rate parameter (probability of reaction).”

**6. Bonding** A free Link element can form bonds with singly bonded and free Links amongst its neighbours as long as the resulting bond angle is greater than or equal to ninety degrees.

**7. Rebonding** Neighbouring cells around a cell which contain either singly bonded or free Links attempt to form bonds amongst themselves until no more bonds can be formed. A bond can only be formed if the resulting bond angle is greater than or equal to ninety degrees.

## Research Questions: Life-Span, Cycle Size

If Autopoiesis is considered a basis of Life (Varela et al., 1974) then questions regarding properties of autopoietic entities become pertinent. By an “entity”, we refer a closed loop of bonded links since it is only then that the an organization similar to a cell emerges (Niebur, 2008). Specifically we ask 1) how “stable” are the entities over time in the presence of inevitable breakages and repair and 2) how large can entities grow during their life span. In both these questions, we are interested to know how configurations of the universe relate to such properties. We name these properties *Life span* and *Cycle size* respectively.

The configurations we would like to vary are 1) the ratio of Holes, Substrates and Catalysts in the starting state i.e. grid configuration and 2) the disintegration probability.

## Experimental Setup

We run two kinds of experiments. One to get an intuition of how entities are born and die and another to collect statistics on how different ratios of Holes, Substrates and Catalysts (H, S, K) and different disintegration probabilities ( $P_d$ ) affect life span and cycle size. Note that production probability is related to disintegration probability as  $P_p = 1 - P_d$ .

**Visualization** We start with a grid configuration (H, S, K) in the ratio 10% : 88% : 2% and disintegration probability 0.02. Using the above parameters, we run for grid sizes  $10 \times 10$ ,  $20 \times 20$ ,  $50 \times 50$ . Results are presented in Figures 2, 3 and 4. Note that loops which are formed only by the apparent crossing of link bonds are not considered entities. To be considered an entity, if we start with any constituent ( $L_d$ ) and follow bonds, we should reach the same ( $L_d$ ) eventually. Thus, entities can be detected and tracked automatically in our system.<sup>5</sup> The crossing of bonds is a phenomenon also seen in (McMullin, 1997, p17) and he notes that “in the absence of some constraint to the contrary in the algorithm, we must assume that it is intended to be allowed.” Indeed, we see an such an entity with cross-link formed in Figure 3.

<sup>5</sup>Note: In the present experiments with our implementation Autopoiesis System (release 0.9.0), there is currently no check whether a catalyst  $K$  is enclosed by this closed cycle, though it would be desirable to add this technical check.

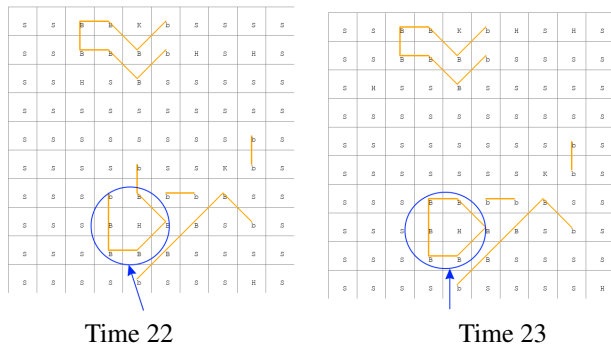


Figure 2: For grid size of 10x10, genesis of a unity with membrane boundary about to form at time 22. Singly- and doubly-bonded links are shown in colour. Complete entity forms (in the bottom center of this universe) at time 23 (circled in blue colour). Note each time instant is here is a ‘snapshot’ of the dynamics, with possible movement of elements and breaking and reforming of links between the these instants. S stands for Substrate, H for hole, K for Catalyst, L for  $L_f$ , b for  $L_s$  and B for  $L_d$ .

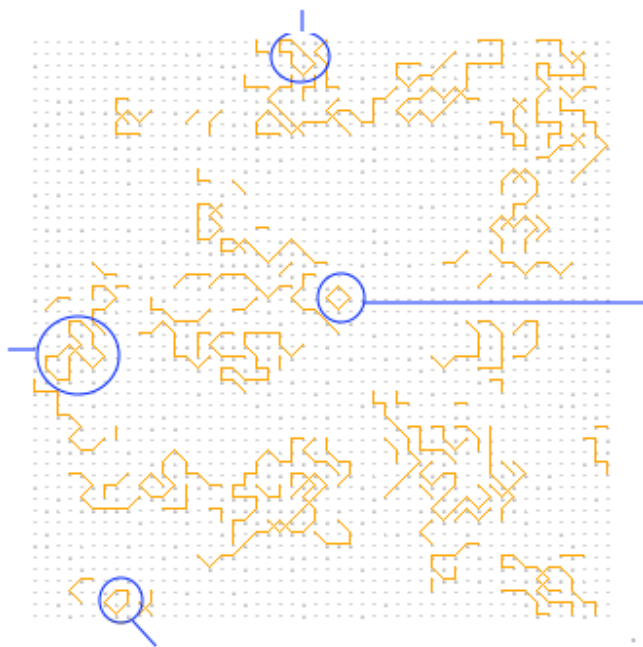


Figure 3: Snapshot of a 50x50 grid at a particular time. Note there are four entities present circled in blue for clarity. Also note that the entity mid-left is considered a single entity even though bonds appear to crisscross each other.

### Collecting Statistics from Multiple Initial Configurations

The overall experiment is run for different initial ratios of Holes, Substrates and Catalysts (H, S, K) and different disintegration probabilities. We run the above on a grid size of  $10 \times 10$  as in (Varela et al., 1974). Additionally we run the same experiments on grid sizes of  $20 \times 20$  and  $50 \times 50$ . The

details of each experimental run is as follows.

- A ratio of (H, S, K) is chosen.
- A disintegration probability is chosen.
- A grid configuration for a given number of Holes, Substrates and Catalysts is generated randomly.
- The simulation is run for 100 or 1000 iterations.
- 25 such simulations are run to get statistics.

The statistics are collected automatically in our simulation implementation which has algorithms to detect entities and measure their life span and cycle size.

**Varying the initial grid configuration** We vary the initial distribution of H, S and K percentages in a given grid in a manner indexed by  $i$  according to the formula: For each  $i$ , a multiple of 5 with  $0 \leq i < 50$ :

$$H = 9 + \lfloor i/2 \rfloor, S = 90 - i, K = 1 + \lfloor i/2 \rfloor \quad (4)$$

The disintegration probability is clamped at 0.02 for this part of the experiment.

**Varying disintegration probability** In this case, the (H, S, K) ratio is clamped at 9% : 90% : 1%. We vary the disintegration probability from [0.02, 0.1].

## Results

We come back to the research questions posed before, namely how the Life span and Cycle size of entities depend on initial grid configuration and disintegration probability. From Figures 5, 6, 7 we see that both mean and standard deviation of Life span and Cycle size remain fairly consistent across different initial grid configurations. From Figures 8, 9 and 10 we see that increasing the disintegration probability affects both Life span and Cycle size negatively. Life span decreases quite starkly on average as disintegration probability increases but more interestingly the standard deviation also decreases, signifying that very few entities will break the average to be long-lived. Average Cycle size, on the other hand, decreases more gently with increasing disintegration probability but here also we see a similar pattern to Life span i.e. As disintegration probability decreases, fewer entities will tend to be very large compared to the average. An overall interesting aspect from Figures 5, 6 and 7 and Figures 8, 9 and 10 is that the boxplots are heavily skewed in the first quartile thereby making the lower whisker invisible. This is an interesting aspect of the distributions that needs to be analysed further.

## Conclusion

We find that the initial grid configuration, i.e. the ratio of holes, substrates and catalysts in a grid does not affect the Life span and Cycle size of entities meaningfully. This is surprising at first but can be explained by the local nature of the reactions (1), (2) and (3) in forming autopoietic entities.

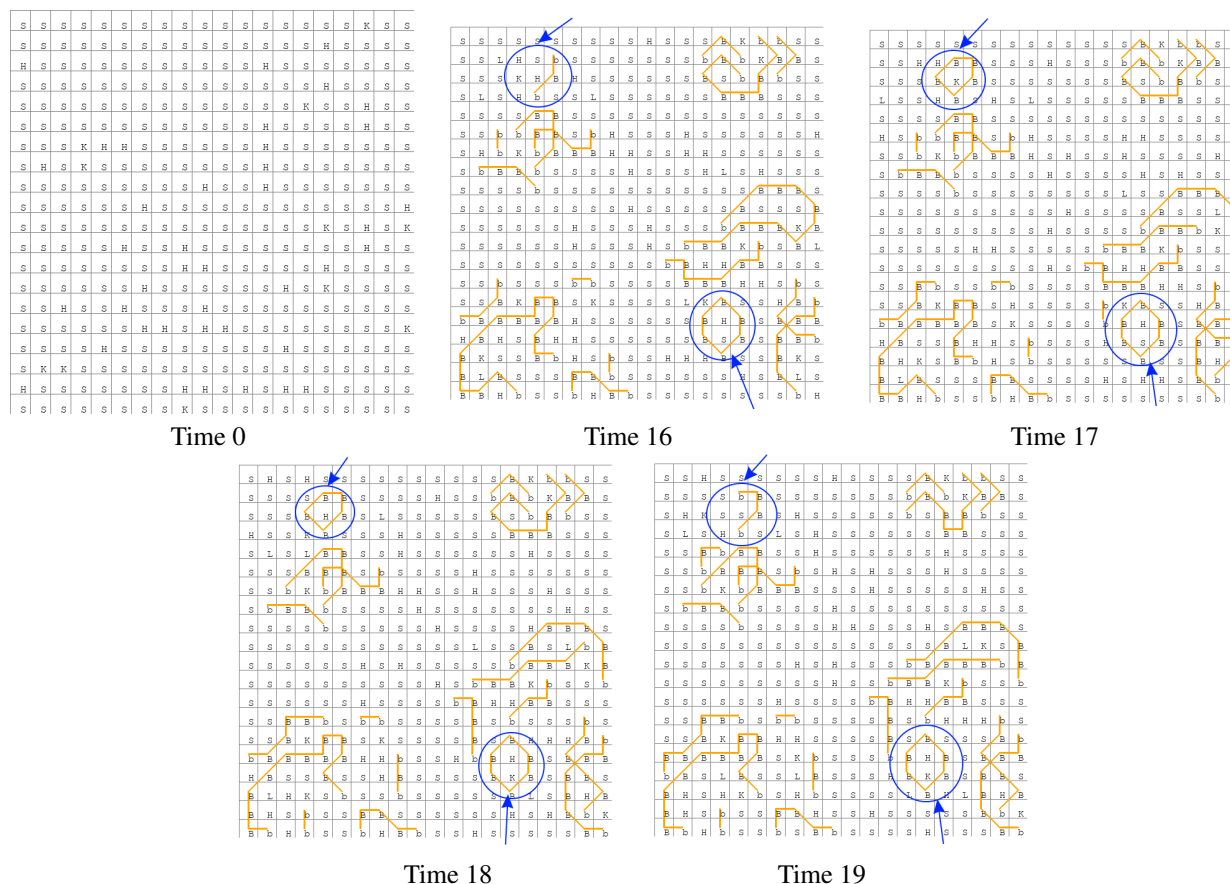


Figure 4: For grid size of 20x20, time evolution of entities at different timesteps. Time 0: Initial configuration with random placement of Holes, Substrates and Catalysts, no Links (free, singly- or double-bonded) are yet present. Membrane boundary about to form at time 16. Singly- and doubly-bonded links are shown in colour. Complete entity forms (in the upper left of this universe) at time 17 and contiguous topological boundary persists through time 18, with loss of spatial closure at time 19. During this genesis and demise of that entity, another entity persistently maintains its organizational closure and boundary in the lower right quadrant.

As neighbours continue to interact and react according to these reactions, autopoietic entities eventually and robustly emerge in disparate conditions e.g. starting out with only one catalyst or dispersed substrates. What is needed is time. As intuition would suggest, if the basic reaction rates are altered e.g. production and disintegration probabilities, then Life span and Cycle size are affected. Life span is more sensitive to disintegration rates than is Cycle size which is robust in its distribution. Moreover, longer runs and larger spaces create “room at the top” for some individuals with longer life span or larger size, respectively.<sup>6</sup> This investiga-

<sup>6</sup>The original description of the seminal Varela-Maturana-Urbe (1974) computational model of autopoiesis was later critically examined and re-implemented by McMullin with the help of Varela to reproduce the phenomenology displayed in that work. This required using *chain-based bond inhibition*, an undocumented mechanism of the original implementation, also not described in the specification by McMullin (1997) on which our implementation is based. Chain-based bond inhibition prevents bonding of any free

tion hints that complex life-like systems can emerge robustly out of simple rules acting locally. More comprehensive exploration of the parameter space (ratios of holes, substrates, catalysts; production and disintegration probability of link elements) would enhance understanding of the range of possible dynamics of computational autopoiesis for our system and other possible models (e.g. 3D variants more similar to phospholipid bilayer bound vesicles studied in synthetic biology and origins of life). Investigations of possible self-reproduction and interaction of autopoietic entities on the basis of the original autopoietic model could also be carried out in future work with our implementation and variants.

$L$  particle in the neighborhood of a double-bonded  $L$ , and greatly increases the self-repair capacity of membrane bound entities (McMullin and Varela, 1997). While not present in the version of our Autopoiesis System (release 0.9.0) investigated here, it would be natural and straightforward to add this inhibition rule as a next step and to study how it impacts both self-organization and life-span of autopoietic entities.

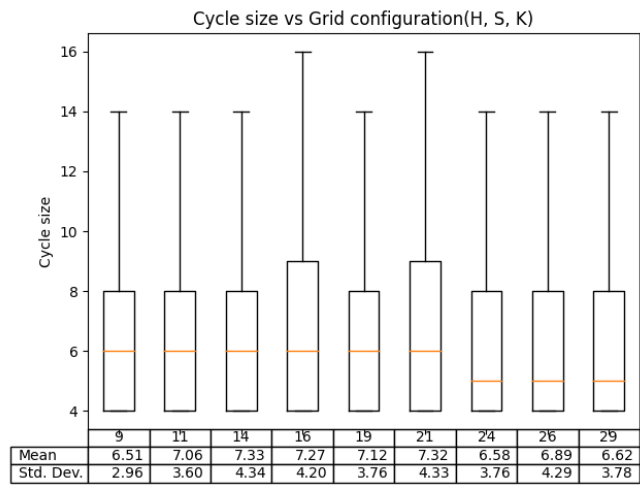
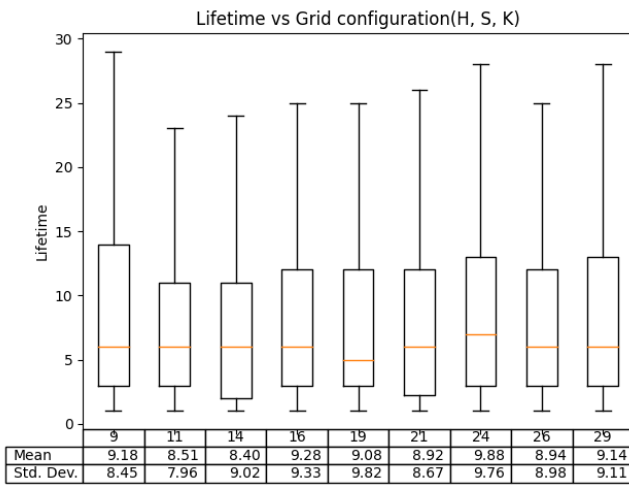


Figure 5: Boxplot for grid size 10x10 and 100 iterations, x-axis lists number of Holes. Both Holes and Catalysts increase at the cost of Substrates. Increasing number of Holes and Catalysts does not appear to affect Life span and Cycle size meaningfully.

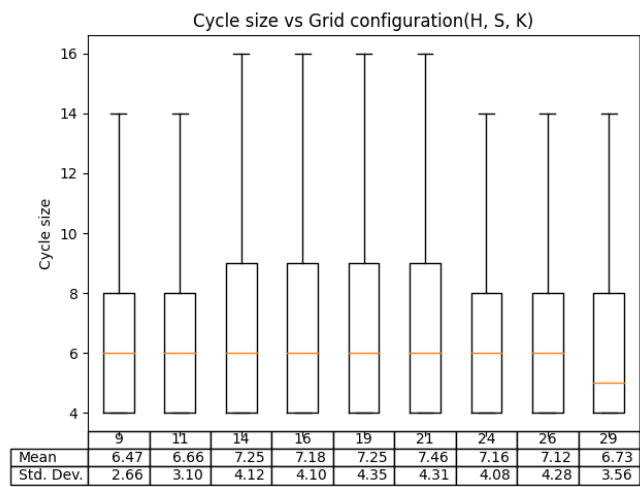
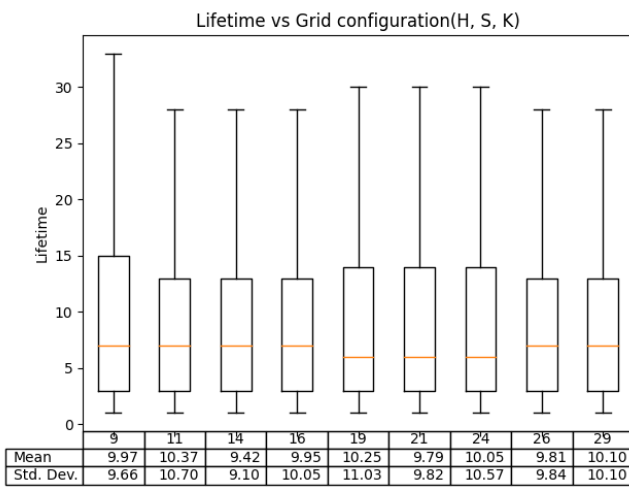


Figure 6: Boxplot for grid size 10x10 and 1000 iterations, x-axis lists number of Holes. Both Holes and Catalysts increase at the cost of Substrates. Results are similar to Figure 5.

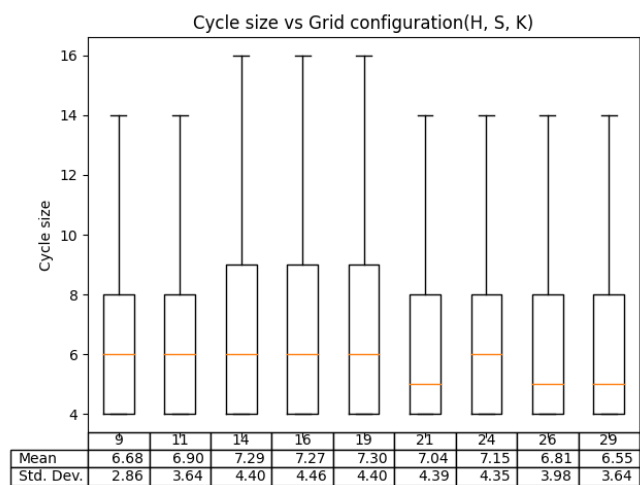
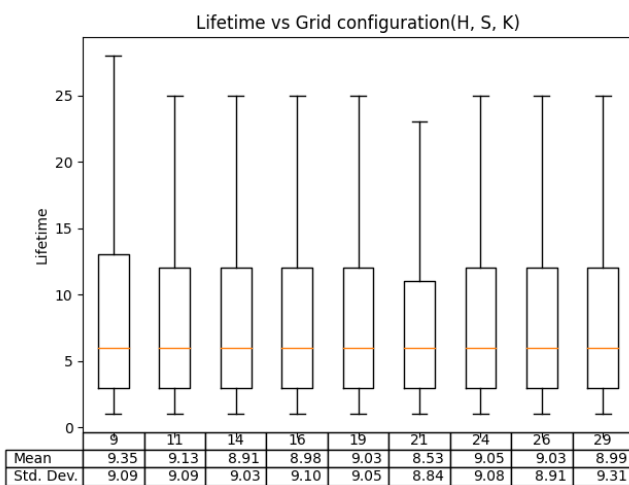


Figure 7: Boxplot for grid size 50x50 and 100 iterations, x-axis lists number of Holes. Both Holes and Catalysts increase at the cost of Substrates. Results are similar to Figure 5.

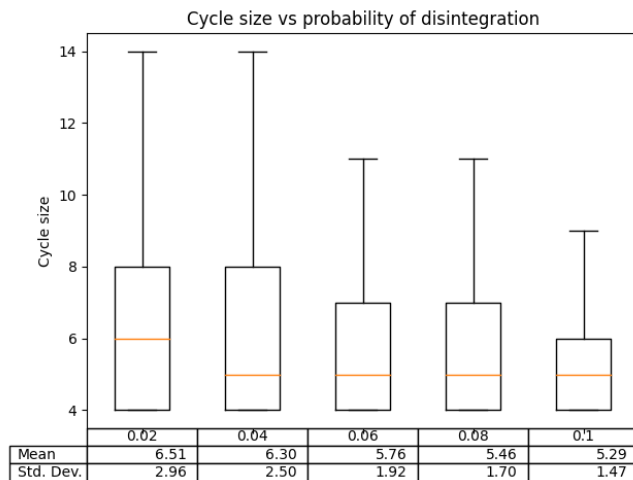
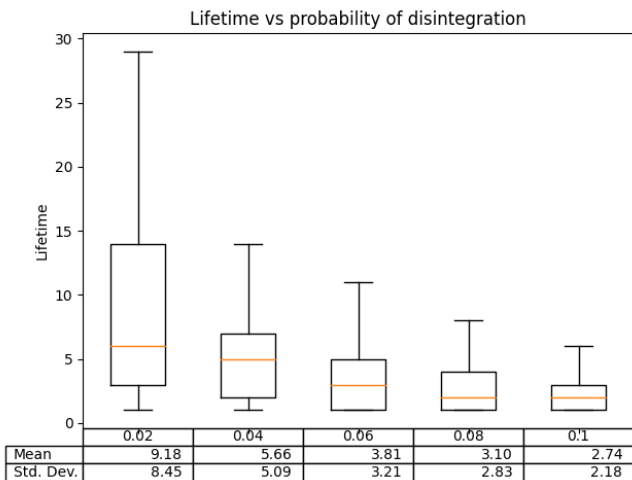


Figure 8: Boxplot for grid size 10x10 and 100 iterations, Probability of disintegration appears to affect Life span inversely quite strongly. Cycle size is also affected in a similar manner though not as strongly.

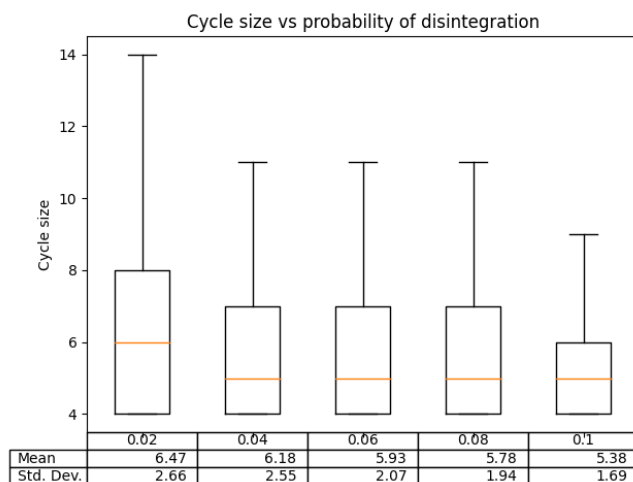
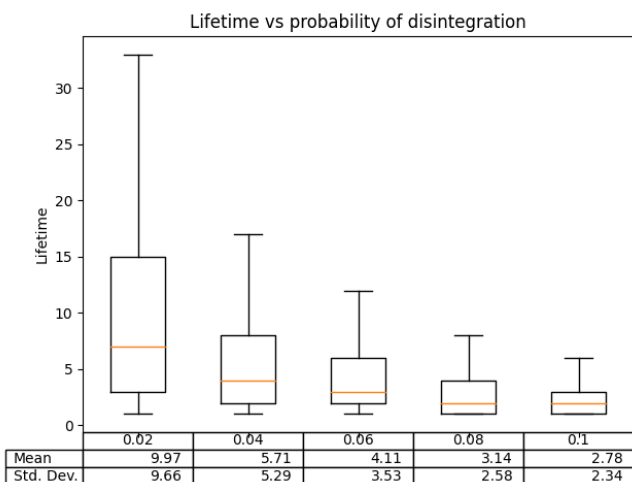


Figure 9: Boxplot for grid size 10x10 and 1000 iterations. Results are similar to Figure 8.

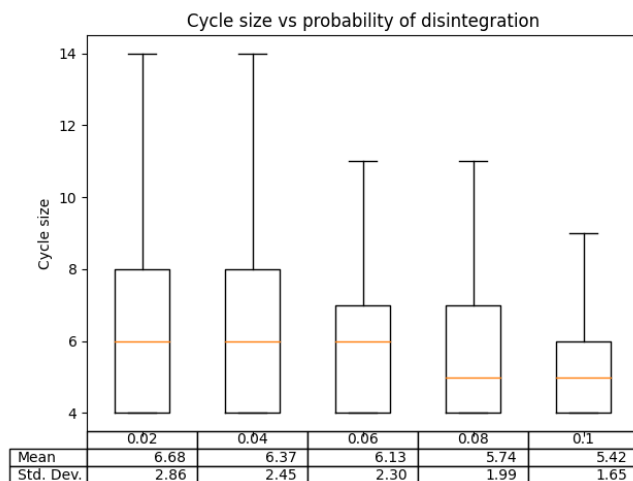
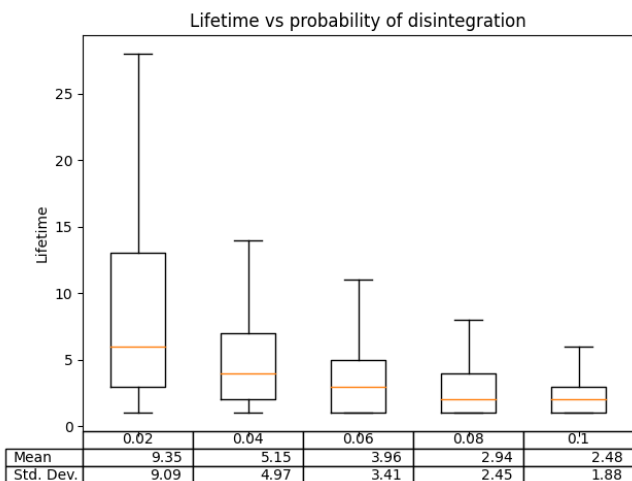


Figure 10: Boxplot for grid size 50x50 and 100 iterations, Results are similar to Figure 8.



## References

- Bachmann, P. A., Luisi, P. L., and Lang, J. (1992). Autocatalytic self-replicating micelles as models for prebiotic structures. *Nature*, 357:57–59.
- Bachmann, P. A., Walde, P., Luigi, P. L., and Lang, J. (1990). Self-replicating reverse micelles and chemical autopoiesis. *Journal of the American Chemical Society*, 112(22):8200–8201.
- Bitbol, M. and Luisi, P. L. (2004). Autopoiesis with or without cognition: defining life at its edge. *Journal of the Royal Society Interface*, 1(1):99–107.
- Bourgine, P. and Stewart, J. (2004). Autopoiesis and cognition. *Artificial Life*, 10(3):327–345.
- Langton, C. G. (1984). Self reproduction in cellular automata. *Physica D*, 10(1-2):135–144.
- Luisi, P. L. (2003). Autopoiesis: a review and a reappraisal. *Naturwissenschaften*, 90:49–59.
- Maturana, H. R. and Varela, F. J. (1980). *Autopoiesis and Cognition: the realization of the living*. Reidel.
- McMullin, B. (1997). Computational autopoiesis: The original algorithm. In *SFI Working Papers*, volume 97-01-001. Santa Fe Institute. <http://www.eeng.dcu.ie/~alife/bmcm9701/>, (Accessed on 05/01/2020).
- McMullin, B. (2004). Thirty years of computational autopoiesis: A review. *Artificial Life*, 10(3):277–295.
- McMullin, B. (2013). Computational autopoiesis. In Dubitzky, W., Wolkenhauer, O., Cho, K.-H., and Yokota, H., editors, *Encyclopedia of Systems Biology*, pages 461–464. Springer New York, New York, NY.
- McMullin, B. and Varela, F. J. (1997). Rediscovering computational autopoiesis. In Husbands, P. and Harvey, I., editors, *Proceedings of the Fourth European Conference on Artificial Life*, page 38–47. MIT Press.
- Niebur, E. (2008). Electrical properties of cell membranes. *Scholarpedia*, 3(6):7166. revision #139387.
- Oros, N. and Nehaniv, C. L. (2007). Sexyloop: Self-reproduction, evolution and sex in cellular automata. In *Proc. IEEE Artificial Life*, pages 130–138.
- Priya, S. (2020). priyasiddharth/autopoiesis: Autopoiesis System. <https://github.com/priyasiddharth/autopoiesis-system/>. (Accessed on 04/30/2020).
- Ray, T. S. (1992). An approach to the synthesis of life. In Langton, C. G., editor, *Artificial Life II*. Addison-Wesley.
- Sayama, H. (1999). A new structurally dissolvable self-reproducing loop evolving in a simple cellular automata space. *Artificial Life*, 5(4):343–365.
- Sirmai, J. (2011). A schematic representation of autopoiesis using a new kind of discrete spatial automaton. In *Advances in Artificial Life (ECAL 2011)*. MIT Press.
- Sirmai, J. (2013). Autopoiesis facilitates self-reproduction. In *Advances in Artificial Life (ECAL 2013)*. MIT Press.
- Szostak, J. W., Bartel, D. P., and Luisi, P. L. (2001). Synthesizing life. *Nature*, 409:388–390.
- Varela, F. J., Maturana, H. R., and Uribe, R. (1974). Autopoiesis: The organization of living systems, its characterization and a model. *Biosystems*, 5(4):187–196.
- von Neumann, J. (1966). *Theory of Self-reproducing Automata*. (Edited and completed by A. W. Burks). University of Illinois Press.
- Zepik, H. H., Bloechliger, E., and P.L., L. (2001). A chemical model of homeostasis. *Angewandte Chemie*, 40:199–202.