## the WINNOWER

### REDDIT

# Science AMA Series: I'm Sijbren Otto, professor of Systems Chemistry. Today we would like to talk with you about complex mixtures at the interface between chemistry and biology and how far we have progressed towards making life in a test tube! AMA!

### SYSTEMS\_CHEMISTRY R/SCIENCE

Hey Reddit! I am Sijbren Otto, joined today by Gaël Schaeffer (postdoc), Andreas Hussain and Jim Ottelé (PhD students) to discuss systems chemistry[1] and synthetic life. You can find a video describing our research here!

Back in 2010 we reported a system where self-replicating molecules spontaneously emerge from a complex mixture, via angrowth breakage mechanism.[2,3] A few years later, we discovered another system using the same concepts, but where mutations lead to the consecutive emergence of two 'species' of replicators, one being the ancestor of the previous one, thus mimicking an important process in biological evolution.[4] This work received a fair amount of attention from the media and from you guys on reddit.

Our next challenges are the incorporation of more biological features into artificial systems, such as adaptation, Darwinian evolution or metabolism and compartmentalisation, in order to one day make a chemical system that captures all the essential elements of life! For more information, visit our group website here or our list of publications here. We are very happy to answer any and all questions relating to this topic.

[1] J. Li, P. Nowak, S. Otto, J. Am. Chem. Soc. 2013, 135, 9222-9239.

[2] J. M. Carnall, C. A. Waudby, A. M. Belenguer, M. C. Stuart, J. J. Peyralans, S. Otto, Science 2010, 327, 1502-1506.

[3] M. Colomb-Delsuc, E. Mattia, J. W. Sadownik, S. Otto, Nat. Commun. 2015, 6, 7427-7433.

[4] J. W. Sadownik, E. Mattia, P. Nowak, S. Otto, Nat. Chem. 2016, 8, 264-269.

Edit: Thanks a lot for all the questions! We are overwhelmed by the amount of good questions right now. We are on to answer some more!

Edit 2: Thanks again for all the questions, we've all had a lot of fun! However, we're in the Netherlands and our dinner is getting cold. We hope to come back in the future, and get some more feedback from you all!

#### • READ REVIEWS How many "generations" can self replicate? Is there any "data loss" that limits the replication, similar to telomere shortening in biological cells? Are there benefits or disadvantages in the "traits" of the ✓ WRITE A REVIEW separate species (one can replicate/one can't, etc)? CORRESPONDENCE: DATE RECEIVED: **DrScroops** February 25, 2017 We use the formed replicator from previous generations to obtain fast replication in a 'fresh' sample. DOI 10.15200/winn.148794.40666 This means that we technically do not observe any "data loss". Our systems have no telomers (which are themselves a product of evolution). Replication can be repeated for many cycles, and we see no ARCHIVED:

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CITATION: Systems\_Chemistry , r/Science decrease in efficiency. However, when we work in systems where mutations can take place, ancestry of specific replicators can be important.

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credited.

What do you think is the minimum complexity required to make a system "alive"? Obviously it has to self-replicate, but there are other requirements, like maintaining homeostasis.

### -Metacelsus-

We believe that if a system can replicate/reproduce, has a basic form of metabolism (through which it maintains itself far from equilibrium) and is physically separated from the environment (compartment/membrane), it should not be too far away from being alive.

As a youth interested in the biochemical field, where and how should I get my start so I can help with projects like these?

### tallbigtree

In our group most people are coming from diverse direction of chemistry. Most of us studied traditional chemistry with emphasis on organic chemistry but we also have people with polymer science nanoscience backgrounds.

How strongly does your research rely on looking over nature's shoulder? Have you ever considered experimenting with molecules never used by nature?

### **SOberhoff**

We borrow concepts from Nature (the traits of Life). We use similar interactions that are found in Nature, therefore parts of our molecules are "natural", but some projects also use fully artificial building blocks not used in nature.

I saw on your website one of your first publications was in 2010. Obviously, this is a long term project.

My question to you is: how far are we from creating cell life, or something similar? Will it take another 6-10 years, or longer?

Thank you very much for your time and all the effort you put into your research.

### \_guy\_fawkes

This is a very good question. We cannot predict how long it will take creating life made by fully synthetic building blocks. We made recent advances in incorporating more features in our system such as death and adaptation but we are lacking some other basic features (compartmentalization). Putting all features essential to life together in a single system will be still the main challenge that is likely to take at least another decade, but probably much more...

Relating to the new planets just found, how would a discovery with your work affect how the exo planet scientists judge whether the environment of the discovered planets may hold life?

### pchancy3

I think we can only answer this question reliably once we have made life based on an alternative biochemistry. Until then, however, I would say that the conditions under which our replicators work are

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not very different from the ambient conditions on Earth, so there it has little impact on how to define habitability.

Thanks for doing this AMA! I have many questions, but I'll just pick two. 1) What would it take for you to call what you are creating "alive"? I don't imagine that you'll be using the 8 characteristics of life. 2) What is the next step after creating these self replicating molecules? What is your current research looking into specifically?

### spinach\_nipplesalad

1)Currently, we are going for a system that shows besides self-replication, compartment formation and some kind of primitive metabolism, in such a way that these processes are coupled to each other via common molecular species – so far only 3 characteristics out of 8.2) Currently we are working at the metabolism part, e.g. replicators that can maintain themselves only upon feeding with a fuel. In a related project we are working on self-replicating compartments formed from similar building blocks. Holy grail is to enable our replicators to exhibit open-ended evolution; i.e. the ability to invent new functions.

What's your personal motivation towards creating life from chemistry?

What's a project you can see becoming a possibility 5 or 10 years down the track?

### **NotPornAccount**

I seriously considered studying paleontology, but decided for chemistry based on the better job prospects. After serendipitously discovering self-replicating molecules I can now earn my living studying evolution, which used to be only a hobby.

Do you use any sort of biological catalysts in your systems Chemistry? Biological systems use enzymes and opposing pathways paired together to maintain complex systems... Do you have any analogous mechanisms you are studying?

### ohailmhic

No. However, we have started a project to give our replicators an additional function; being able to catalyze a chemical reaction. The plan is that when a replicator forms and starts to grow, it should start to show catalytic activity towards a certain reaction. We have done preliminary experiments in which the fibers can catalyze ester hydrolysis. The next step is for these fibers to be able to catalyze the formation of their own food. Opposing pathways is also something we are actively exploring (very good questions!) and which seems to produce interesting results.

Hi there! I've got two questions:

1) What are the biggest hurdles you have to overcome in your work and where could you see this work leading in the future?

2) Do you think it could be possible that a different and perhaps more efficient central dogma of biology could be produced or even exist?

Thanks!

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### Panzerforce

- There are several hurdles we are facing. For example, in order to allow Darwinian evolution to go places (invent new functions) we have to sweep through a large multidimensional space of physical parameters that can influence the process and success is probably on found in a small part of this space. From a technical point of view, we would like to go for higher complexity (e.g. multicomponent libraries) but then we run into problems concerning chemical analysis and tend to compromise replication ability.
- 2. A different biochemisty perhaps! Would be fantastic and we will definitely try an push our systems in this direction. A better biochemistry I doubt it. Hard to best >3 billion years of evolution.

A great deal of polymer chemistry is seen in biological systems. DNA polymers can be up to 2m in length, while peptide polymers bond, interact and fold to do a function.

My question, what are the length, molecular weights and strength of (what appeared from the YouTube sketches) your synthetic replicating polymer? Also, what kind of protein-like characteristics do they have if any?

Edit: question marks

### carefullycalibrated

The synthetic self-replicating polymers are 150-200 nanometers long. The molecular weight of one self-replicating molecule is 4500-5000 Da. One polymer chain contains ca 300-400 macrocycles, so the weight is about 40-80 kDa. The replicator molecules are held together by beta-sheet type interactions which are common in protein chemistry. About the strength of the interactions : we only have data from simulations and the interaction strength between two replicator molecules is estimated to be ca. 120 kJ/mol.

As biochemists, to what extent do you anticipate being able to account for the emergent properties of life in your research? After all, it's a big leap from discovering some self-replicating molecules to synthetically imitating even the simplest prokaryote. How does your team break down this massive project into manageable chunks? Do you set incremental goals, etc.?

### <u>Awomir</u>

We would not define ourselves as biochemists; we are organic/supramolecular chemists. But it is indeed a huge step from self-replication to simple Life in a test tube (which, in turn, is still far away from prokaryotes). We are using a bottom-up strategy, implementing our self-replicating system to get it closer and closer to alive. We are not there yet, but we hope that Darwinian evolution will help us (it has done it before)... :-) Note that breaking life down into manageable chunks might not work: life is an emergent property that disappears upon breaking it down into parts.

How limited are self-replicating (transcription error joke) systems in terms of environment (pH, temperature, substrate availability, pressure, etc)?

### logically

At the moment pretty limited, we are working in relatively narrow temperature and pH ranges, in water (or with a small fraction of a co-solvent). Also, small modifications on the substrate can have a big influence on whether replication will be observed or not. Overall our systems are more resilient than many life forms, but not quite as robust as some others.

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If any of you are religious or spiritual, have these kinds of experiments affected your beliefs? Do they make you feel like a God? Do they undermine God? Or do they give you a new appreciation/understanding of your faith?

Not sure I totally understand the bio of what you guys are doing, but I feel, even if just single-cell bacteria was created in my lab, it would really change my perspective on things.

### hurrikaneerikkson

Firstly we are still very far from making a cell but rather work with simple molecules which can show some traits of life. But indeed, we would also be rather moved should we get to the point that what we have in our test tubes would quality as living. Whether it would resemble a cell is an interesting question. We are not sure it necessarily would...

How far away are we from having RuBisCO's enantiomer? How about an entire mirrored cell? Both seem like they'd be neat.

### N4MayShun

As far as I can understand you asking whether we can make life in a different chirality. We indeed can change the chirality (i.e. make the mirror image) of our replicators and everything still works fine. We are still far away from a full-fledges cells though...

How far are you planning on taking this? How complex will this artificial life get?

### Noy\_Telinu

The difficulty in answering this is that one cannot foresee how complex those systems are going to become. We like to push them as far into complexity as they want to go, given that complexity is likely to harbor the most exciting new functions.

### Fascinating!

What would you characterize as "the essential elements of life?" In other words, how do you define a living thing because it seems as though it can be somewhat subjective.

Thanks! Y'all are the future!

### **Pharcy**

It is extremely difficult to define life, especially since we have such a small frame of reference (earth). However, we must start somewhere, and we believe that something alive must exhibit three ingredients; replication, metabolism, compartmentalization and be maintained far from equilibrium. Once one of our systems has shown these properties simultaneously, we can discuss whether or not it is alive ;-)

Should you succeed in creating life, what will it be called? For that matter where exactly would this fall into classification, in an existing group or in something entirely new?

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### Tephra022

Thinking of a name would be a cool challenge! For now we use "de-novo life" (Craig Venter already claimed synthetic life). Nice to dream about a new category in the systematic classification...

Using systems chemistry, can you build reactivity in a way similar to the structural evolution you've shown? That is, can you evolve a system to select for a certain reaction/catalytic process? If so, is the reactivity demonstrated unique to the sum of the components?

Your work has huge implications in most, if not all, fields of chemistry, what applications are you most excited for?

### marrowtheft

We are currently working on a system that shows emergent catalysis, when the replicators emerge and grow, they show catalytic activity towards, for example, ester hydrolysis. This could lead to very interesting applications such as oscillating systems, the deprotection of precursor molecules, parasitic behavior of other species and maybe even an actual hypercycle. We've only just started this project, and the main challenge so far is to link catalytic activity to replicating ability (the latter is the only thing we can readily select for). We are most excited about the prospect for open-endedness, where anything can happen.

Fascinating research by your group! I think your line of research will yield great insights into how life arose.

I am very interested in systems applications to scientific questions, with Systems Biology being my particular interest.

Do you all see systems analyses (e.x. Systems Biology) as the future of scientific research? I am very high on the future of Sys Bio in the field of Biology, and I wonder if you all share the same anticipation (so to speak)?

### Bacobi1

Complex systems (in biology, chemistry or other fields) are very promising areas for future research. At the moment, systems chemistry is not as advance as systems biology and synthetic biology but hopefully with the help of other research groups we will be able to change that in the future. And we fully agree with you that that future is bright!

I'm a physics students thinking to go into Origins of Life research for grad school. In general, how much of what you do directly involves physics?

### <u>Ibman</u>

Since our systems become quite complex and hard to predict we try to involve quite some amount of computer modelling. This is something which is currently needed in the field and you are well suited with a physical background.

### Good stuff!

I had a question about the linked video (the one about the 2010 Science paper) and the study on which

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it is based. Is it different from a simple one-pot synthesis of such supramolecular structures in the way that formation of the final product (the stacked rods) actually causes more formation of the building blocks (the individual rings) which in turn results in more of the product, whereas most one-pot synthesis studies of nanostructures do not focus on continuously shifting the equilibrium towards the building blocks? This is the impression I am getting from the video and the abstract (I cannot access the paper at the moment).

Would it be allowed for you to upload a free PDF of the paper online?

Please let me know if my question isn't clear.

### tongguost

Please drop us an e-mail.

How far has your progress come since 2010?

### **MySocksFit**

We have proven that the replication in this system is exponential (necessary for Darwinian evolution by replicators under most conditions), we have increaded the complexity/diversity of the system (mixing different types of building blocks), we are very close to observe adaptation to the environment and create a primitive form of metabolism and run replication far from equilibrium. We still need to couple these features in a single system.

Wow, this is a very ambitious project. My question are: if human actually manage to prompt molecules into creating life, should we start "inoculating" planets?

### <u>bihobi</u>

Interesting thought.. Lots of ifs and buts, and very far from being practical right now ;-)

Wow! I've been a bit dissilusioned with the mostly reductionist approaches in Science, so it's refreshing to see your research, which is truly creative and integrative by highlighting the fundamental nature of complex adaptive systems and shifting the ontological focus from the analysis of physical elements to the synthesis of evolutionary interactions, which is a perspective that could breathe new life to all fields of study. Thanks!

### InfinitePS

We couldn't agree more! Thanks :-)

Thank you very much for this AMA! This is a topic that I find fascinating.

Chemists are very confortable playing with systems that will reach equilibrium. The events that occur while the system is changing towards equilibrium are important to know if you want to understand how to better control a reaction, but it is not absolutely necessary to know them to design a reaction as long as you understand the thermodynamic stabilities of products and reactants.

Living things do not follow this rule. There are constant inputs from the environment keeping the system out of equilibrium, and most of the magic of life occurs while the system is changing rather than

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when a thermodynamic minimum is reached.

My question is the following:

How good are chemists now at modelling and controlling systems that remain out of equilibrium, and how does your team deal with these non-equilibrium dynamics?

### <u>Tnemirepxe</u>

The complete answer will come out in the form of a review article in Chem Soc Rev soon. You are completely right about the necessity of out of the equilibrium processes in Nature. We are working hard to get our replicators to work under conditions of continuous energy dissipation (i.e. out of equilibrium) and believe this is the way forward!

Hello! Thank you for this AMA! As a student who is interested in the biochemical field as well, I would like to ask for a general idea on how do you plan to apply Darwinian Evolution to these artificial life? What are the possible selective pressures that can be applied to these artificial, technically-not-alive, life?

Not sure if mentioned but, how closely are the artificial life based on actual life (regarding both the chemical and biological composition of actual life)? What kind of results did tests using other types of chemicals yield?

Thank you!

Side note: since it's not technically natural selection, what type of selection process would you call this? O.o

### LucriaDeEclipse

By working in systems containing different types of building blocks (see Sadownik et al.), we can introduce mutation in our replicators. Then if we can introduce a selection process (fitness in a given environment) under conditions that replication and replicator death occur concurrently, we are not far from Darwinian evolution (mutation/selection based). Indeed we already observed adaptation to a changing environment, albeit rather trivial. Note that replications works with both natural and unnatural building blocks (i.e. the principles hold well beyond the molecules selected by contemporary life!)

What applications to society do you foresee with this technology?

### **Pharcy**

This is fundamental research; making synthetic life could have infinite possibilities. It is impossible to say what we could do, but when we discussed it with each other we thought it would be cool if the life we create can 'eat' the bubblegum from the streets ;-) On a more serious (but still science fiction) note: if we were to succeed in making life then we could perhaps use it to replace chemical factories; this time the factories would be tiny and make themselves and repair themselves...

would your research be able to help prove that somewhere in the universe life could be established not my oxygen and water but of something else like sulfur or something crazier?

### Novaraa

Well, the replicators that we are creating actually require both water and oxygen! However, there are

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some bacteria that can survive without oxygen, and some species can even exist in the harsh conditions of a vacuum (tardigrades). If our research is successful in the creation of synthetic life, that could mean that other types of life are possible, not excluding life that requires water.

Is this work revealing anything about how life may have started on earth/ how it might start on other planets?

### Darth\_Balthazar

Our work reveals some general principles that could (but need not) have played a role in how life originated on Earth and elsewhere.

How complex is the mixture the self-replication happens in? Could such a mixture form by itself under reasonable circumstances? Have you investigated whether you can simplify the mixture somehow and still achieve self-replication?

### <u>amaurea</u>

Our mixtures are actually quite simple! We start from a limited number of very simple building blocks that can form rings and start replicating. A mixture such as this is highly unlikely to form by itself (we pay a lot of money for our building blocks!) and how such mixture could have emerged on a pre-biotic earth (for example) is still a mystery. Making mixtures simpler (less diverse) usually makes it easier for replicators to emerge.

What implications can this have in the real world? How can we use these discoveries?

### <u>Huntguy</u>

I think we've answered your question more or less here.

Dear Dr. Schaeffer and Prof. Dr. Otto,

This type of research you do is incredibly valuable in both that it will allow us to understand the origin of life at a much deeper level, and that it in the far future we may be able to literally synthesize life.

I am a Masters student now and in a couple years I see myself trying to get funding for fundamental research in chemistry. It worries me to constantly hear that it is nearly impossible to obtain grants for this type of work. Clearly it is not impossible for you!

Can you share any strategies you have used to secure funding for the type of work you do?

Also, are there any projects that you would really like to work on but have not been able to due to a lack of funding?

Thank you!

### **Chiropterotriton**

Fundamental science, if significant, appealing and well presented, can certainly attract funding. Helps to have something that is conceptually new to stand out from the crowd.

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What brought you to, or interested you in, your current research? Additionally, what did the path to your current research topic look like?

### Calovichi\_Otter

Originally, we used the same chemistry to create artificial receptors (hosts) for small molecule guests, i.e. from a dynamic combinatorial library of molecules, one molecule is preferably formed (amplified) because it interacts with an externally introduced guest molecule. The replicators were discovered purely by chance. However, their formation is also based on interaction between molecules; just in this case it is not the interaction of a library member and a guest molecule that leads to amplification, but that between the library members themselves.

Let's say you're eventually successful and create an organisms de novo.

Do you kill it, keep it under a high level of containment or risk letting it get out into the wild?

### **EtOHMartini**

Firstly we are talking about molecular systems which are below the cell level. So far our systems needs very special molecules as "food" which are not found in nature. Furthermore it is extremely unlikely they are able to compete with the much more advanced organisms that currently inhabit Earth.

How and what ethical issues are addressed relating to this kind if chemistry? Is any life / cells you create subject to any rights?

#### pob\_91

It is probably a bit too early to talk about ethics, but as we are getting closer and closer to artificial Life, but for sure a discussion that will go beyond the simple chemical question will arise eventually (but this is probably still decades away).

This is an incredible topic, thank you for doing this AMA.

What are the timescales involved with these sorts of generations? Could they be accelerated to the point in which the evolution of the systems take place in such a way that generations could spring up in moments?

Essentially I'm asking if these experiments could get out of hand. If you create a system that garners a generation every second or few seconds, and that somehow got exposed to a natural environment on earth capable of sustaining the system, could a new, possibly invasive, form of life be produced?

I know this borders along the lines of science fiction, but I think whenever one grapples with the idea of self replication, topics like this are hard to avoid.

#### **TheBlackLagooner**

It can take up to 3-4 weeks for the replicator to emerge and be the main species in one of our samples (the rest being food). If we add some of the replicator from a previous generation, this conversion can be completed within hours. You don't have to worry about these replicators 'eating our world' because the food that they need to grow is extremely specific. Even molecules that look very similar but have one different peptide in their tails could cause the system to stop replicating. Furthermore, biology had a headstart of several billion years and catching up and making something that is competitive with contemporary life is extremely unlikely. Even if things would "escape" simply bleach would destroy it.

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Thanks for doing this AMA. I always found it curious that some of the more polar compounds are nucleic acids, and that their binding homologues are aminoacids which when aggregated form proteins and thus creating complex molecules which life is based upon. My question is the following: Is there any indication that the self replicating molecules replicate following a polarity gradient? (more polar form slightly less polar). My biochemistry is shaky at best so forgive any errors in my assumptions.

### **DaRealGeorgeBush**

The success whether a molecule self-replicates depends on the secondary interactions between them. This happens in a certain window of polarity: if the building blocks are too apolar, the resulting macrocycles simply aggregate in a non-specific manner (or if they are too apolar, they simply don't dissolve in water). On the other hand, if they are too polar, they prefer to interact with water instead of themselves. In between, we have the chance of finding a building block that forms self-replicating macrocycles. In principle, we can create a gradient: inducing self-replication of molecule A (which is too polar to replicate) by adding a small amount of replicator formed from molecule B. In this way, we can make self-replicators of molecules that in themselves would not replicate. There is an ongoing project in this topic currently in our group.

What kind of applications are there for this?

What relationship does your research have with biosensors?

### speisenkarte

We are far away for any applications (and it is a good question to see what they could be!). At this moment, we don't see any connection with biosensors.

Those threads in the video reminded me a lot of wormlike micelle solutions (amphiphilic molecules that form flexible, but fragile, cylindrical structures with the hydrophobic tails on the insides and the hydrophilic heads on the outsides). Do they have anything in common, or is it just a consequence of the simplification into a cartoon form that makes them seem similar?

### N8CCRG

The similarity between our replicators and wormlike micelles is certainly there. There are also some differences to note: Micelles are held together purely by hydrophobic interactions, whereas in the replicator stacks also hydrogen bonding between the peptides plays a role. Most important different is, however, that in our system te surfactant monomers are formed from smaller components by covalent (disulfide) bond formation and that this process is driven by the assembly of the resulting molecule into the micelle-like stacks.

Considering we're advancing in both branches - A.I and scientifically produced biological life- how do you feel these would co-exist in the future?

### notacephalopod

At the moment (and possibly for a long time), they are well separated fields. Maybe there will be a way to merge them in the future... Intriguing thought!! But also somehow scary to give AI a physical form that goes beyond a computer :-)

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Is the approach based more off combinitorial chemistry where many approaches are tried at once or more from trying to predict what sort of system would replicate and running fewer experiments?

### justin6543

We attempt to design our system in a more or less rationale manner (i.e. not mixing random building blocks and waiting for an interesting outcome), but unfortunately, the systems are so complex (many different kind of secondary interactions, mechanosensitivity, formation of nanostructures, eventually micelles, etc) that we cannot apply rational design beyond a certain extent. That is, we have a rough idea about what criteria the system has to fulfil in order to do operate in a certain manner, but these criteria can be satisfied by numerous different combinations, so we apply a focused trial-and-error approach.

What sort of environments can your molecules operate in? And would you be able to make ones that exist in harsh environments (e.g. highly acidic/alkali and extremes of pressure)?

### Suidan3

Our molecules operate in slightly basic aqueous medium (but remain functional down to pH 2-3 but strong base is not good!). we also studied the effect of organic co-solvents and found that the presence of certain co-solvents can induce the emergence of new replicators from the same building block (see our paper from 2015:<u>http://pubs.acs.org/doi/abs/10.1021/ja512644f</u>). We haven't examine the effect of high pressure yet.

What are your thoughts on the idea that life arose because it was the most thermodynamically stable state under the conditions it was in? If this is the case would this imply that not only is it possible for life to exist on earth-like planets, but it might even be inevitable in places with similar conditions? Thanks for doing this AMA!

### **TheSupernaturalist**

We think that the main characteristic of a chemical system that can lead to life is not its thermodynamic stability, but its capability to evolve and adapt already on the chemical level. In principle, life is a far-from equilibrium system, and if it reaches equilibrium, it tends to be dead. Of course, life cannot be based on too unstable molecules, but among the many relatively stable ones, the main selection criteria is not a thermodynamic one. I'd recommend reading the papers by Addy Pross on the concept of dynamic kinetic stability. See: <a href="https://jsystchem.springeropen.com/articles/10.1186/1759-2208-2-1">https://jsystchem.springeropen.com/articles/10.1186/1759-2208-2-1</a>

How close are we to Gattaca?

### InthegrOTTO87

Gattaca is about genetic engineering (and designer babies), not synthetic life. This research doesn't have much to do with this in a direct way since it's not about manipulating DNA or anything like that. Also we are not as handsome as Ethan Hawke.

Do you think that the artificial systems that you create will eventually evolve quicker or slower than natural evolution happening on Earth?

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### <u>janxyz</u>

We believe that the artificial systems that we create may initially evolve much quicker compared to natural evolution given the fact that we deal with systems that are much simpler. But I doubt we will ever overtake current life, as replication speed tends to slow down as systems complexify.

How excited should I be that a dystopian future brought about by mad scientists is right around the corner?

### **MisterSquirrel**

The dystopian future around the corner depends more on electoral preferences than our activities ;-)

Can someone do an ELI5 on the fly for me? What do you consider life? What does this mean for the average person? What type of life can be created?

### iHateDem\_

The definition of Life is a good one. Replication/reproduction(make copies of itself), compartment (contained within a shell of some sort) and metabolism (can convert food into bits of itself) connected together should not be too far off from Life. For the average person, it means that we are trying to make a system that contains all the traits of Life, but probably not in the form that we currently know. Given that we only know one type of life, this one would be a second, and hopefully a very different one.

Have you been able to synthesize any compound that early life could have used as a medium to turn light (or radiation) into usable chemical energy?

### matruschkasized

No, but we also haven't tried!

Can you tell if a seed is "alive" - that is capable of growing? Is there a way to know before planting?

### <u>imiiiiik</u>

Difficult to answer. Indeed dead seeds and viable seeds are probably very hard to distinguish. This shows how thin the line is that separates life from death...

How or what would form the basis for conscience, intelligence etc in such a life form?

### moontails

Conscientiousness requires a brain, and our replicators are still very far away from a cell, let alone a fully functioning organism!

Probably not your field of expertise but maybe you can answer, will this work help develop artificial life (i.e. Robots) that can regenerate itself through bio-mechanisms? If not then do you think that

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### technology is far off?

### MuricanTragedy5

Our current systems do not interface with robotics nor with biology, and establishing such interfaces requires a lot of effort.

Have you looked into silicon based life? I'm Chemical Engineering student. Just curious about anything involving silicon.

### bickster69

No, we remain within conventional organic chemistry ;-).

how appealing does the technology of CRISPR look to Ph.D. holders like you guys?

### s0upsandwich

CRISPR is VERY interesting for geneticists; however CRISPR is specific to biological cells. Our systems will not react to any CRISPR since it contains no DNA sequences.

Thanks for doing this AMA! My question is about the CRISPR-Cas system and what role you think this might play (if any) in creating "life in a tube". It's my understanding that this technology might allow for targeted genomic editing and manipulation. Does that have any applications here, or is that perhaps more applicable for transitioning or re-designing existing organisms?

### \_DanceMyth\_

CRISPR-Cas system is indeed specific to biological cells and DNA, so it would not do anything in our systems (which does not have DNA). It would only have applications for organism using double stranded DNA.

This seems pretty cool research! Would a goal of this research be to create a new genetic code? Also creating life in a test tube - could this be used to support the panspermia theory of how life started on earth?

### bored-of-work

Decoupling genotype from phenotype as achieved through the genetic code would be a very nice thing to have, but at present our systems are very far from it.

Great work, I have two questions, First, do the molecules developed/used in this experiment exist in nature or were they uniquely developed in lab in an attempt to achieve the desired results. If they were designed, presuming that you are able to say, what processes were used in the development of said molecules.

### <u>qna1</u>

The very same molecules do not exist in nature, but of course, similar oligopeptides (as a substructure of larger structures) do exist. The design originally aimed for beta-sheet forming molecules , but within



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the same molecule and not between two different molecules. To achieve beta sheet formation, the (very simple) design principle was to have a short alternating chain of apolar and polar amino acids. However, we can replace the peptides by completely synthetic parts and the system still works!

What kind of benifits can we get from test tube life?

### **KingNosePicker**

Another form of Life would help to define Life (at the moment, only based on one type). And creating a new sort of Life is a great challenge on its own. Having systems that copy and repair themselves might supplement the current chemical products nicely.