

**Some general system properties of a living observer
and the environment he explores**

Thomas Dandekar^{1,2}

¹Department of Bioinformatics, University of Würzburg, Biozentrum, Am Hubland
D-97074 Würzburg; and ²EMBL, Postfach 102209, D-69012 Heidelberg, Germany

e-mail : dandekar@biozentrum.uni-wuerzburg.de

Tel. +49-(0)931-888-4551

Fax. +49-(0)931-8884552

Gott III (1993)¹ started from a human observer and made a number of witty conclusions about our future prospects. In the same spirit, we derive implications for “the meaning of life, the universe and all the rest”² from few principles. Adams’ absurd answer² “42” tells the lesson “garbage in / garbage out” - or suggests that the question is non calculable.

We show that experience of “meaning” and to decide fundamental questions which can not be decided by formal systems imply central properties of life: Ever higher levels of internal representation of the world and an escalating tendency to become more complex. An observer, “collecting observations” and three measures for complexity are examined. A theory on living systems is derived focussing on their internal representation of information. Living systems are more complex than Kolmogorov complexity (“life is NOT simple”) and overcome decision limits (Gödel theorem) for formal systems as illustrated for cell cycle. Only a world with very fine tuned environments allows life. Such a world is itself rather complex and hence excessive large in its space of different states – a living observer has thus a high probability to reside in a complex and fine tuned universe.

(Life:) From experience we discover basic principles³. Complete explanations of the world (“theories of everything”; TOE) rely on dualisms⁴ (e.g. light and dark) or monisms (e.g. “panta rei”, all is in flux; Heraklit⁵). More accurate, the standard model⁶ in physics considers the transformation of all four basic forces in nature. It agrees well with observations. However, it is a description of the universe in which no life is assumed. No particular “meaning” of the universe is apparent, only different transformations of forces into each other. How can such a theory produce any results for life or offer meaning to an observer?

This brings up the non-trivial task to formalize life and “meaning”. To encompass all aspects of life in any closed or formal form is exceedingly difficult and will in general produce a non-calculable result. Furthermore, it is perhaps not very satisfactory to introduce “additional” principles to the standard model – is not life after all (at least to the materialist) completely explainable by the physical principles already summarized in the standard model? Instead, we will focus on central emergent properties of life. These are not apparent from the basic physical building blocks (leptons, field quanta etc.) but result as system behaviour. To derive the concept of “meaning” in a scientific or biological context we have to concentrate on the *escalating properties* of life (“life multiplies and fills up ecosystems; man invents and learns the use of fire, atom bombs and microchips” - a cynic would say “the suicidal properties” of life):

Life is autocatalytic, collects information on the environment to improve its survival and easily establishes a next level of complexity (Fig. 1).

The formalism 1 (supplementary Material) describes this and exploits that both in biology and physics transition probabilities can describe central properties. Furthermore, it can directly be applied to study system behaviour even in complex biological systems (Fig. 1S). In particular, living beings experience their environment by interacting with it. There is a feedback of sensory input from motor input and only correct actions in the environment satisfy the internal drives and needs of the living being. This creates slowly a reliable internal representation of the outside world⁷. Only in such an operational context of living and acting in an environment you can really experience *meaning* (e.g. hunger, “thirst, milk, grab it”, desire, satisfaction etc.; Fig. S3b). These central properties allow living beings furthermore to question their own foundations (Fig. S3a). This is in contrast to closed and formal exact systems (such as typical computers; Gödel theorem, see e.g.⁸⁻¹⁰).

(“*meaning*”:) However, why should living beings be any different (in particular as they are composed of the same basic building blocks)? Well, firstly our everyday experience tells us that human beings can constantly ponder over their foundations, they can decide on complex questions, ethical values, aesthetics and philosophy. This is no self deception: Living beings are in their genetic or neural information storing actively gathered information on the environment they are in, which in turn is part of the next larger environment, and so on until the foundations of the world itself (formalism 1). As these last foundations (the “Platon” limit) shape both natural selection and also our concept of meaning as well as our concept of our own foundations they allow us to reflect about our own principles. A technical system which is sufficiently alive* would also be able to reflect about its foundations.

Living beings can question their foundations as their internal representation of information and their own survival is selected in an open and infinite context.

Formalism 2 (suppl. Mat.) formalizes this: Mutations depend among other things also on gamma rays from a very distant quasar hitting the earth and our DNA. Furthermore, our concepts of logic, time, mathematics etc. do not found on miraculous *a priori* truths (“*synthetische Urteile a priori*”; Kant) but rather biological selection made sure (e.g.¹¹) that the very basic foundations of our universe are mirrored in our neurobiology and genetics. Interestingly, we find that complex decisions beyond the Gödel limit are possible and resolved stochastically (Fig. 2; box G, Fig. 3Sa): Even then there is no stalling of the living system as besides internally representing information, each molecule has also biochemical activity and the probabilities for the resulting system behaviour and states are selected for optimal survival.** Furthermore, this system properties are a modern way to rephrase Sokrates¹², who tried by questioning people having a problem that they discovered what were

the deeper reasons and natural principles behind their questions.*** Instead of a vague and philosophical search for a or even “the” “meaning of life” we may more appreciate that “meaning” itself occurs as a systems effect in a living observer (Fig. 1; Fig. S3b). Thus life has as one central feature its creativity implying more than enough potential to identify an observer dependent “*meaning*” of all and everything.

(“*the universe*”:) Just the same, life as such could still be useless, a rare accident, negligible compared to the vast universe¹³. An alternative view is the anthropocentric principle: If there is an observer (e.g. us) then fine tuned conditions have been selected to assure that conditions are favourable for life and an intelligent observer. All other less ordered universes[&] simply are not observed because no observer can exist in them. This principle and its variations¹⁴ make plausible that e.g. (i) an ozone layer exists, (ii) a stable and yellow sun shines on our planet for billions of years and (iii) carbon exists in this universe stable and with four valences because most variations of these and many other basic features would ban life from this planet and from the rest of our universe.

Nevertheless, such an argument is a bit ad hoc (it depends on that we are already there). Furthermore, it identifies besides general principles for any intelligent existence many specific features necessary for our existence but not necessary for every kind of intelligent observer¹⁵. Moreover it implies that we are the lucky observers in a rare world[&] whereas in myriads of others worlds chaos rules and no life can exist (“Multi-verse” containing rare worlds where life is possible; e.g.^{15,16}). Koonin¹⁷ stressed this idea recently in a radical version: Critical improbable steps for life (e.g. replication or translation machinery) will happen for sure in an infinite expanding and budding inflationary multi-verse where anything at all possible happens with certainty in at least one of the local buds (“universes”). However, this only claims that even the most improbable may happen. Worse, it creates an uneasy feeling: Are we that one in a gazillion chance? What are we missing here?¹⁸. This is in fact

very similar to the astonishment about the extreme fine tuning of the physical constants¹⁶. Importantly, this hurts the Copernican principle¹: Life and an observer would be considered to happen very rarely and to be very, very special.

(“... *and the rest?*”) However, most of the less favourable universes[&] are simple and without much structure. Formalisms such as Kolmogorov complexity¹⁹ help to see, that most universes which are chaotic can be described in a very short form. In contrast, worlds which are most creative (which most easy can give birth to something new such as new ideas or life or new observers or new environments etc.) are exceedingly complex and take the biggest slice of the total state space Omega (Fig. 3; details in Table 1S, Table 2S). There is no fine tuning of nature’s basic constants necessary¹⁶ for our world where such nice things as life and a human observer can exist. Instead only a very fine tuned universe becomes exceedingly complex and gets by this property also a large slice of Omega (the space of all possible). An earlier theory postulated that a hypothetical “reproduction rate” of a world[&] would be connected to the rate of black hole production¹⁵. Our hypothesis is independent of such ad hoc postulates (note also²⁰). Furthermore, it fits nicely to the openness of string theory²¹: Of course very many worlds and types of physics are possible and compatible with nature, but only a very fine tuned world is exceedingly complex and thus includes life and us (Tables 1S, 2S):

In general, worlds or environments which are more complex require more fine tuned parameters and a more complex description (see formalism 3, suppl. Mat.). However, this corresponds in fact to a bigger slice in Omega, the space of all possible states and worlds. That is the reason why observers (we!) on average happen to be in a world which is quite creative and creates among its other creative activities something as complex (or weird) as life.

The fine tuning of nature's constants would thus be no accident. Worlds have a particular big slice of the space of all possible states only if they are escalating increasingly complex^{&&}. Life has a chance in them. It is one of their most creative consequences with exactly such properties. This allows us to exist and prosper, to look successfully for deeper insights and meaning and to discover such and other principles.

Notes: This is a discussion paper / preprint (1st version July 2007)

& A "universe" or "world" denotes here a specific set of natural laws and natural constant settings in the abstract space of all possible sets of settings

* This implies (i) all its deductions are selected by natural selection and survival in an open environment; (ii) the system is open and biologically fuzzy - in contrast to a closed and formal system. Axioms alone do not build a mathematical theory. The systematic combination of axioms produces myriads of uninteresting statements. Only a creative mathematician (or another living being) looks for interesting statements (meaningful statements require to experience meaning - which again requires critical features of a realistic environment, suitable desires and suitable training as well as evolution and adaptation).

** Concrete decisions despite their infinite context happen in living beings not using a renormalization formalism⁶. Instead, building blocks are limited and a neuronal or genetic decision happens in finite time; the infinite context is only coarsely mirrored.

*** A question is only asked as long as the person posing the question is still not content – and not until truth is reached. Criticizing the questioner and straighten out definitions shows fundamental drives behind a question and the environmental context in which the drive makes sense. An example is death and the wish for survival: DNA information, culture and language typically last many generations, ideas maybe eternal, however persons and personal memory are for good evolutionary reasons limited to a few years.

&&Clearly I have the opinion that the world is not simple, e.g. in contrast to ²².

References

1. Gott, J. R. III. Implications of the Copernican Principle for Our Future Prospects. *Nature*, **363**, 315 (1993).
2. Adams, D. *The hitchhiker's guide to the galaxy*. Ballantine Books (ISBN: 0345391802).
Del Rey; Reissue edition (1995)
3. Barrow, J. D. *Theories of Everything*. Oxford Univ. Press (1991).
4. Pretement, S. In: *The dictionary of the History of ideas*. The electronic text Center,
University of Virginia Library. Gale Group, Charlottesville, VA.
<http://etext.lib.virginia.edu/cgi-local/DHI/dhi.cgi?id=dv2-05> (2003).
5. Kirk, G.S., Raven, J.E. & Schofield, M. *The Presocratic Philosophers* (2nd Ed.),
Cambridge University Press (1983).
6. Griffiths, David J. *Introduction to Elementary Particles*. Wiley, John & Sons, Inc. ISBN
0471603864 (1987).
7. Figge, Udo L. Jakob von Uexküll: Merkmale and Wirkmale. *Semiotica* **134**, 193-200
(2001).
8. Hofstadter, D. R. *Gödel, Escher, Bach: an Eternal Golden Braid*. Basic Books;
Jackson, TN (1979).
9. Penrose, R. *The Emperor's New Mind*, Oxford University Press (1990).
10. Penrose, R. *Shadows of the Mind: A Search for the Missing Science of Consciousness*.
Oxford University Press; Reprint edition (1996)
11. Ditfurth, H. v. *Wir sind nicht nur von dieser Welt* (10th edition 1994) Deutscher
Taschenbuch Publ., München (1984).

12. Taylor, C.C.W., Hare, R.M. & Barnes, J. *Greek Philosophers — Socrates, Plato, and Aristotle*, Oxford University Press, NY (1998).
13. Monod, J. *Chance and Necessity*. New York. Vintage paperback ISBN 0394718259 (1971).
14. Carr, B .J. & Rees, M. J. The Anthropic Principle and the Structure of the Physical World, *Nature* **278**, 605-612 (1979).
15. Smolin, L. *The Life of the Cosmos*. Oxford University Press (1997).
16. Barrow, J. D. *The Constants of Nature*, Pantheon Books, ISBN 0375422218 (2003).
17. Koonin, E. The cosmological model of eternal inflation and the transition from chance to biological evolution in the history of life. *Biol Direct.* **2**, 15 (2007).
18. Ball, P. Is physics watching over us? *Nature Science update*, 13th Aug. (2002)
19. Schmidhuber, J. Hierarchies of generalized Kolmogorov complexities and nonenumerable universal measures computable in the limit. *International Journal of Foundations of Computer Science* 13(4):587-612 (2002).
20. Chapline, G. *Dark energy stars*. Texas conference on relativistic astrophysics, Stanford, CA, 12/12/2004-12/17/04 (2004).
21. Green, B. *The Elegant Universe: Superstrings, Hidden Dimensions, and the Quest for the Ultimate Theory*. Vintage Publ. (Bertelsmann), New York, ISBN 0375708111 (2000).
22. Wolfram, Stephen (2002) "A New Kind of Science" Wolfram Media Inc. Champaign Illinois. ISBN 1-57955-008-8
23. Vastrik, I., D'Eustachio, P, Schmidt, E., Joshi-Tope, G., Gopinath, G., Croft, D., de Bono B, Gillespie M, Jassal B, Lewis, S, Matthews, L, Wu, G., Birney, E. & Stein L. Reactome: a knowledge base of biologic pathways and processes. *Genome Biol.* **8**, R39 (2007).
24. Mukherji, M., Bell, R., Supekova, L., Wang, Y., Orth, A. P., Batalov S, Miraglia L, Huesken D, Lange J, Martin C, Sahasrabudhe S, Reinhardt M, Natt F, Hall J, Mickanin

- C, Labow M, Chanda SK, Cho CY & Schultz PG. Genome-wide functional analysis of human cell-cycle regulators. *Proc Natl Acad Sci USA* **103**, 14819-14824 (2006).
25. Chaitin, G. The limits of reason. *Sci Am.* **294**, 74-81 (2006).
26. Ubersax, J. A., Woodbury, E. L., Quang, P.N. , Paraz, M., Blethrow, J. D., Shah, K. , Shokat, K.M. & Morgan, D.O. Targets of the cyclin-dependent kinase Cdk1. *Nature* **25**, 859 (2003).

[26 References]

[main: 1503 words]

[three display items]

Acknowledgements Land Bavaria

Author Information: The author declares no competing financial interests. Correspondence and requests for materials should be addressed to dandekar@biozentrum.uni-wuerzburg.de

Figure Legends:

Fig. 1. Basic and escalating creative properties of life. Life is self generating, either identical or with mutations (M). These properties may further lead to additional levels of complexity (M') or conquer new environments (M''). Additional levels of complexity in living organisms store information (on this next level) by interacting with the environment. Actions lead to new sensory input. Information selected to be stored and survival of a living being depends on the environment which is itself part of a series of ever larger environments.

Fig. 2. Complexity measures examined for cell cycle. Using the software cytoscape, different complexity measures are exemplified for reactome maps²³ (<http://www.genomeknowledge.org:8000/about.html>) of the cell cycle.

Shown is the central biological circuit for the G1 to S transition (in colour different involved proteins). The square in azur shows decision nodes in white and key interactions between them in black according to the reactome software. The total reactome map for the cell cycle contains 356 molecules in the simplified cell cycle model of the Reactome database (map React_152.2). The biochemical key events of decision events are given as a marked list at the right.

Kolmogorov compression endeavours to represent the behaviour of this system by a shorter program giving the desired output (e.g. replicate / do not replicate; thus shortest conceivable but non-predictive trivial model contains one bit), trivial compressions are all representations of the cell cycle using fewer nodes (though the output characteristics would not be identical). Instead the number of genes involved in the cell cycle involves hundreds of genes²⁴ (Kolmogorov complexity in this more accurate model already in the order of tens of thousands of bits).

Moreover, we show in the suppl. material that *no short program* can represent the resulting complexity for the cellular *transition processes* involved, e.g. the transition from G

phase to S phase (**Chaitin complexity**²⁵; participating are 127 molecules, if the network is set up according to the genomeknowledge database). A key interaction is between cyclin E and cdk 2. The program describing this level of complexity is at least as long as the information content of the protein sequences and the regulatory sequences of the genes involved (at least on the order of hundreds to thousands of bits). The non-compressibility can also be shown genetically: All information carrying parts of the system do in fact change the behaviour in case of mutation.

Including interactions renders the complexity even far higher (**O(DNA)** see Table 1S): This is in principle unlimited more complex if all details of interactions are considered including environmental interactions and exact behaviour in time for the cell division program under all conditions. For example, data on cell division kinase 1 phosphorylation targets involve over 500 proteins in yeast²⁶; some of them participate in feedback regulation.

Gödel limit crossing in living systems and in the example network: Non decidable statements or conflicting statements may arise from self referring statements (for Gödel self-referring statements and “arithmoquination”⁸, see Box G). These are here cellular processes states affecting and thus referring to the whole cell, e.g. cell cycle start is promoted according to dephosphorylation of cyclin B-bound cdc 2 for entry into mitosis. However, an inhibitory pathway (e.g. via wee1 catalyzing the inhibitory tyrosine phosphorylation of CDC2/cyclin B kinase) may be activated at the same time: Internally then opposing information is not only represented but in the system opposing or non decidable concatenations (for the internal rules how to represent information; Box G) from such statements can occur. However, as besides the internal representation each statement is also part of a molecular activity, answers happen nevertheless (in general stochastically) and can be e.g. apoptosis, recombination, proliferation etc according to best survival chances in a potential unlimited environment.

Fig. 3. An escalating complex universe takes the biggest slice of Omega and favours among other complex structures life. A “universe” or “world” denotes here a specific set of physical parameter settings (natural laws and natural constant settings) in the abstract space of all possible sets of settings. Omega, the space of all possible environments or worlds contains per definition all basic or elementary states for all worlds. A particular complex world has many basic states. An escalating complex world is creative and as a consequence it favours life and observers. With high chance any observer is in an escalating complex universe, may be even in the most complex one (“world 1”) as this easily outnumbers all simpler universes in possibilities for different elementary states including states compatible with life. In particular, if the state space increases exponential or over-exponential (“escalating complex”) with the number of parameters, the escalating complex worlds take most of the state space. *Data examples* (details in Table 2S): Comparing “worlds” with 1 to 10 parameters yields for a linear increasing parameter space only 10/55 of the state space for the most complex “world” having ten parameters. This can be compared to more than half of the state space (1024/2047) even for the simplest exponential increase in complexity of the state space, the exponent 2. Similar results apply e.g. comparing different scenarios for the relation between basic physical forces (electromagnetic versus weak versus strong force) regarding stability of the atom or proton. Most parameter combinations are rather unstable, in contrast stable solutions allow very large state spaces for all sorts of physical objects as well as for life (example in Fig. 2).

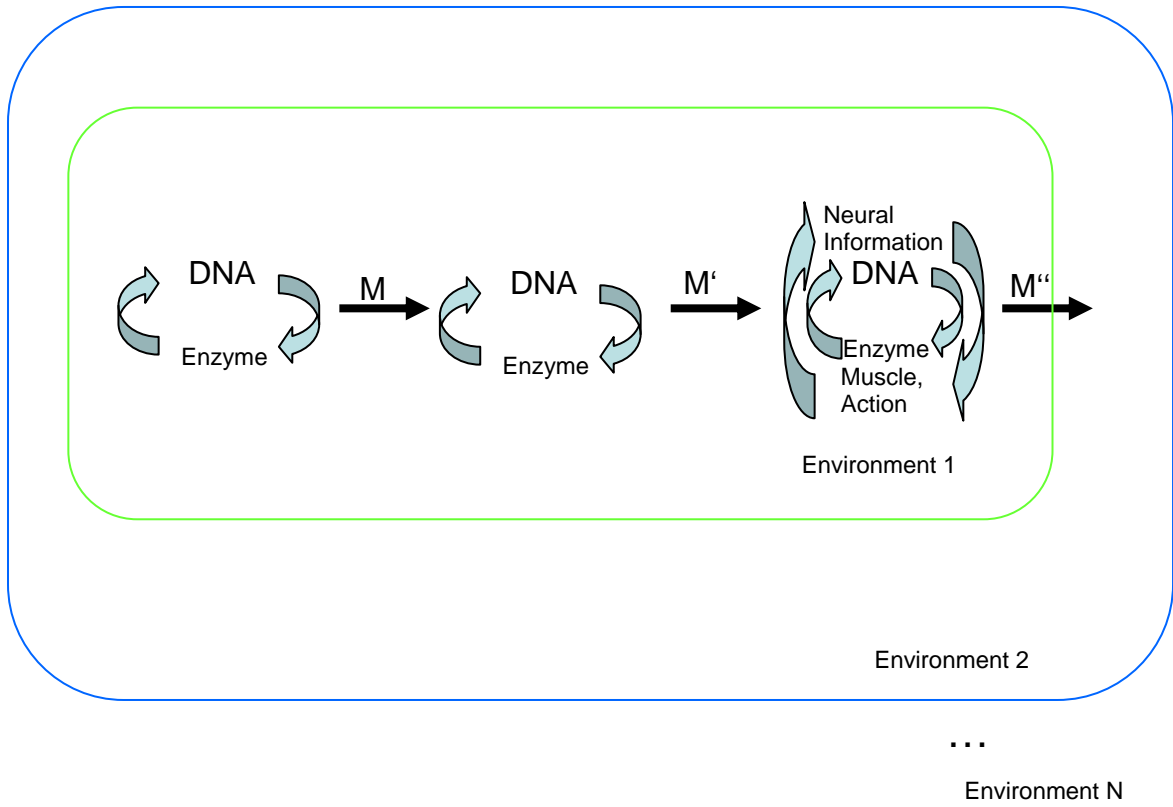
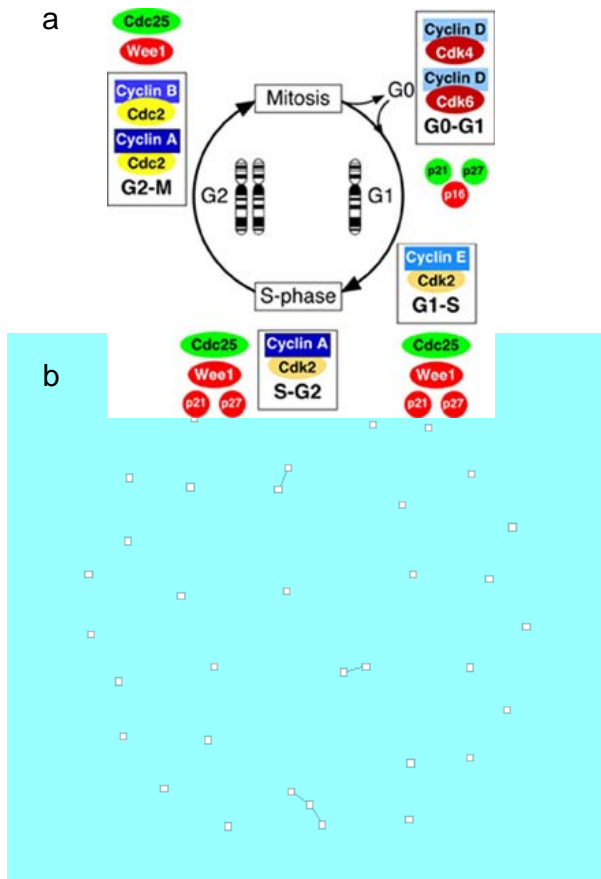


Fig. 1



Cell Cycle Reactome map: Sub-map G to S transition

- ...
- c G1/S Transition**
- c Cyclin E associated events during G1/S transition
 - c Formation of Cyclin E:Cdk2 complexes
 - m Formation of Cyclin E1:Cdk2 complexes
 - m Formation of Cyclin E2:Cdk2 complexes
 - c Translocation of Cyclin E:Cdk2 complex to the nucleus
 - m Translocation of cyclin E1:Cdk2 complexes to the nucleus
 - m Translocation of cyclin E2:Cdk2 complexes to the nucleus
 - c Inactivation of Cyclin E:Cdk2 complexes by p27/p21
 - m Inactivation of Cyclin E1:Cdk2 complex by p27/p21
 - m Inactivation of Cyclin E2:Cdk2 complex by p27/p21
 - c SCF(Skp2)-mediated degradation of p27/p21
 - c Cyclin E/A:Cdk2-mediated phosphorylation of p27/p21
 - m Cyclin A:Cdk2 mediated phosphorylation of p27/p21
 - m Cyclin E:Cdk2 mediated phosphorylation of p27/p21
 - c Association of Cks1 with SCF(Skp2) complex
 - c Binding of phospho-p27/p21:Cdk2:Cyclin E/A to the SCF(Skp2):Cks1 complex
 - c Ubiquitination of phospho-p27/p21
 - c Degradation of ubiquitinated p27/p21 by the 26S proteasome
 - c Phosphorylation of Cyclin E:Cdk2 complexes
 - m Phosphorylation of Cyclin E1:Cdk2 complexes by Wee1
 - m Phosphorylation of Cyclin E2:Cdk2 complexes by Wee1
 - c Dephosphorylation of Cyclin E:Cdk2 complexes by Cdc25A
 - m Dephosphorylation of Cyclin E1:Cdk2 complexes by Cdc25A
 - m Dephosphorylation of Cyclin E2:Cdk2 complexes by Cdc25A
 - c CAK-mediated phosphorylation of Cyclin E:Cdk2
 - c Phosphorylation of proteins involved in G1/S transition by active Cyclin E:Cdk2 complexes
 - c Cyclin E:Cdk2-mediated phosphorylation of Rb
 - c Ubiquitin-Dependent Degradation of Cyclin E
 - c Ubiquitin-Dependent Degradation of Cyclin E1
 - c Ubiquitin-Dependent Degradation of Cyclin E2
- c G1/S-Specific Transcription...**

Fig. 2

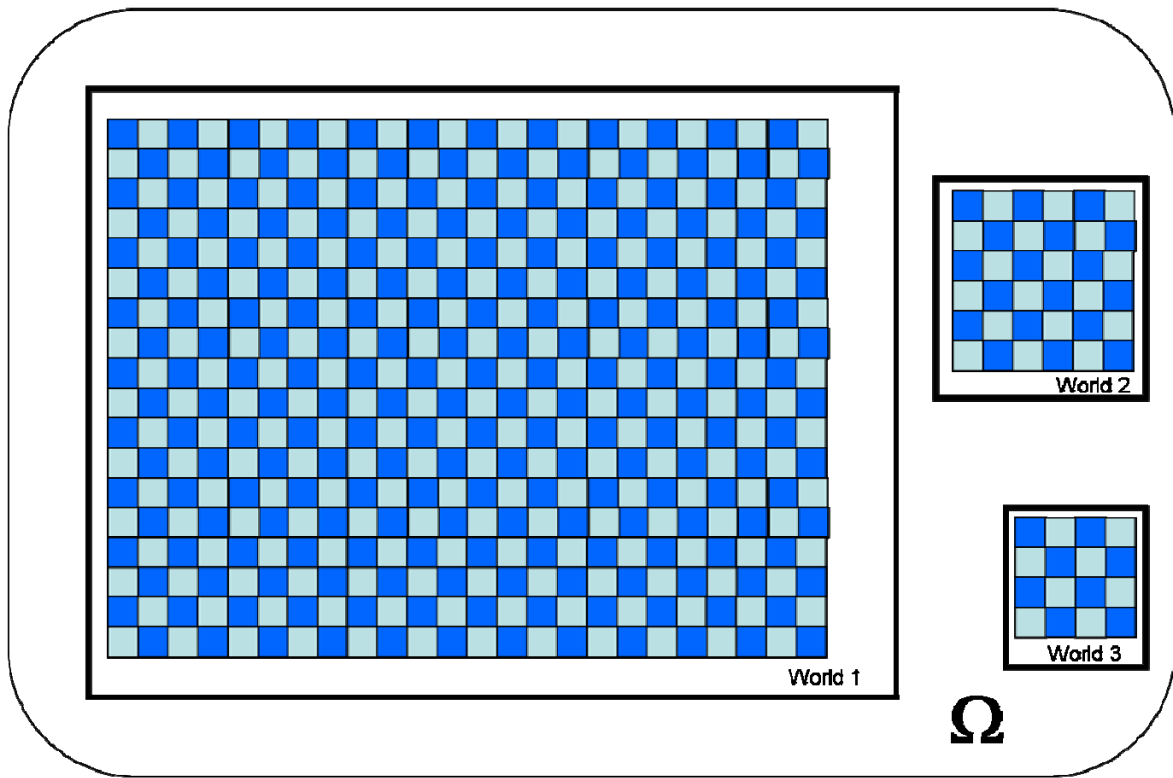
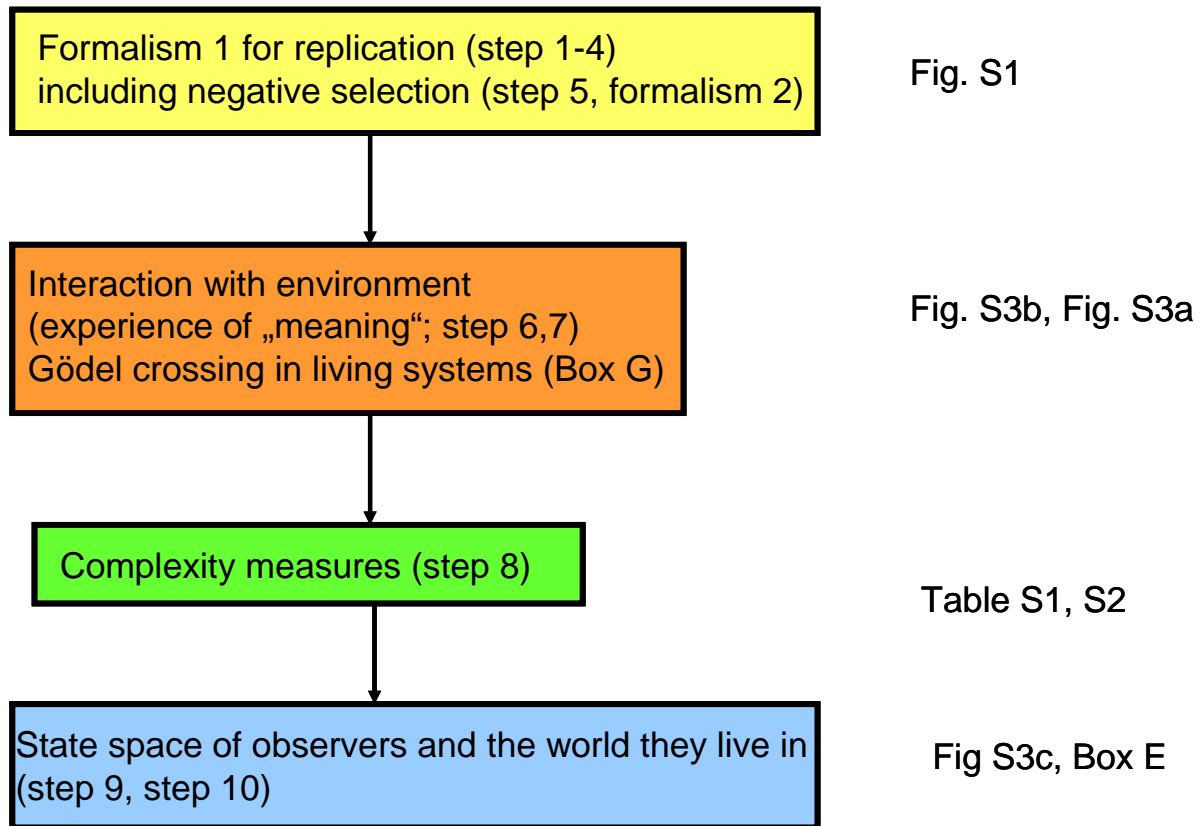


Fig. 3

Supplementary Material: A formalism for life focussing on internal representation of information



Summary (Scheme 1). The flow of supplementary material and the article results is identical and summarized in the scheme above. We focus on one central aspect of life: Its information processing, starting from DNA (step 1). Any fully detailed “theory of life” is of course impossible and also naïve. However, we show that our formalism allows to include quite detailed formal descriptions and results regarding quasi-species, metabolism, perception and higher biological system effects (Fig S1). Part I: We calculate (formalism 1) the probability of a DNA species (step 1) as well as higher levels of life (step 2) to replicate (step 3), mutate (step 4) or be selected against (step 5; formalism 2).

Part II discusses implications (steps 6-10): Simple implications (step 6) and a biological concept of “meaning” as well as the experience of meaning in living beings of sufficient complexity (step 7; Fig. S3a). We show that life, already on the level of the average survival probability of a DNA species can not be represented in a simple way, in particular not by short programs (“compressed”; life is more complex than Kolomogorov complexity) and this applies even more for our complex environment (step 8; formalism 3; Table 2S).

Step 8(iv), 9 and 10 are more speculative implications: Step 9 examines a common framework integrating our theory of information representation in biological systems with fundamental physics exploring transition state formalisms. This allows to draw some analogies between the formalisms used here for biology and some basic formalisms in physics. Step 10 analyzes the concept of “meaning” in different biological species. This allows to conclude that the “meaning” (implying an observer to ask this question, see steps above) of our environment (“universe”) is excessively complex. We discuss the process of observation and include an economic alternative to Everett models (Seligman et al., 1973; Fig. S3c, Box E). Finally, we briefly analyze the concept of the complete space of all elementary states in the context of Platonic philosophy.

The Formalism (steps 1.-5.)

1. Formalism for DNA survival: To support our above arguments and for the fun of it (as it has not really been done yet, has it?), we will sketch here a formalism for live and “meaning” (the latter resulting by internal representation and processing of information in living beings). It is clear that a formalism for life is impossible to give in full detail or explicit. Instead we will first focus on one specific DNA sequence (one individual or clone, a $\text{DNA}_{\text{vector}i}$) and its change during time. We claim that now there are for the first time sufficient data and overall methods available to try to achieve such a goal more rigorously and that this should help in particular also to better explore different types of information and better translate them between biology and physics including important concepts such as the biological experience of “meaning”.

We use transition probabilities as a common formalism both in biology and physics; we include systems behaviour and this leads ultimately to experience, conscience and meaning as emergent properties of the formalism.

The change of a specific DNA sequence during time depends on the replication rate r and the probability for replication $p(r)$, that the sequence is not mutated (m) with probability $p(m)$ and that the sequence is not killed or selected for elimination (s) with probability $p(s)$:

$$d/dt \text{DNA}_{\text{vector}i} = \text{DNA}_{\text{vector}i} \times (r \times p(r)) \times (1-p(m)) \times (1-p(s)) \quad (\text{Formalism 1})$$

Note that for the negative selection s , replication r and mutation rate m detailed studies are already there, yielding detailed quantitative predictions describing well the experimental observations (e.g. Eigen and Schuster, 1979; Bi and Poo, 1999; Schuster et al., 2000; Alvarez-Vasquez et al., 2005; Shamovsky et al., 2006; Iriarte et al., 2004).

In total, there are nn DNA types tried out during evolution and a sub-set n forms a species (if these are only self-replicating molecules this would be a quasi-species according to Eigen, see Emren et al., 2006; Eigen and Schuster, 1979). Certainly also this specific molecule class could be described e.g. according to Schrödinger’s equation (Barrow, 1991). However, this would yield only the detailed vibrations (wave functions to be more accurate) for each electron and all other elementary particles. The dimensions of the DNA molecule are much larger, encompassing many elementary particles. Furthermore, we neglect in formalism 1 specific movements during time and space. Instead, here we look at the change in the *amount* of each DNA species (note that each species is defined by its specific information content in the form of the DNA sequence).

2. A hierarchy of complexity and different types of information stored: To calculate the sub-terms in formalism 1, we next have to take into account, that life has the possibility to form more and more complex layers. We will focus on five levels of layers which form a hierarchy (Fig. S2):

- (1) $\text{DNA}_{\text{vector}i}$,
- (2) Hypercycle from polymerase and supporting enzymes and information encoding $\text{DNA}_{\text{vector}i}$ plus supporting nucleic acids,
- (3) Metabolic flow and regulation within a living cell,
- (4) Cellular and particular neuronal interactions establishing a multi-cellular organism,
- (5) socio-cultural interactions between individuals which form a civilisation.

Each new level of complexity relies on information from the layer below and forms new active units for adaptation to the environment.

If we want to describe the resulting phenotype, we would have:

- (1) $\sum \text{DNA}_{\text{vector}i}$ sum over the n DNA sequences who make up the (quasi)species yielding a 1D-array with individual sequences in each field of the array (in actual fact, in evolutionary old times there was originally only catalytic RNA, but for this the same formula would apply for our purpose).
- (2) Next each $\text{DNA}_{\text{vector}i}$ is replaced by a 2D-Array to describe the components of an autocatalytic hypercycle of nucleic acids and enzymes as the encoded enzyme strings should also be considered (plus catalyzed reactions and products).
- (3) At the level of the cell a further dimension is added by regulation, so that we have genes, enzymes and their regulation on the RNA and transcription factor level: 3D array of sequences.
- (4) multi-cellular organisms would need yet a further dimension for the cellular communication and
- (5) a civilization adds further dimension of inter-individual interactions and communication.

Each next layer has its basic components formed from the lower layer, however, each specific layer interacts with the environment and this interaction allows to store information on higher levels [in 2: Concrete coupling and activities of individual parts of the hyper-cycle enzymes or nucleic acids (Emren et al., 2006, Eigen and Schuster, 1979); in 3: Metabolic flow and regulation (e.g. Schuster et al., 2000; Almaas et al., 2004; Alvarez-Vasquez et al., 2005) including memory effects resulting from previous metabolic conditions or previous transcriptional switches (e.g. heat shock, Shamovsky et al., 2006), in 4: Different effects on cellular connectivity, in particular neuronal connectivity and memory (e.g. Bi and Poo, 1999), in 5: Cultural memory effects, in particular language, culture, tradition and knowledge (e.g. Iriarte et al., 2004)].

It is an important and basic property of life that in course of evolution further dimensions can always be added as the last level of complexity can form new basic components for yet a higher hierarchical level which again according to the emerging new system effects will store information of a new type in the system state of this next level of organisation.

Creativity in life results from ever new DNA species and new information stored as well as new types of information and of processing information (determined by the right hand terms in formalism 1). Creativity results from (i) new levels and (ii) emergent system properties at the same level by varying building blocks and resulting varying system behaviour (e.g. neuronal capabilities: Different sensory qualities and types of perception but also other abilities including painting and music composition result from rather similar building blocks: neurons). In the formalism 1 this corresponds from level 4 and higher to typical human notions of creativity. Note that Igamberdiev (2006) discusses computability from a quantum measurement framework and compares abilities of quantum computers to keep coherent states with the coherent state of living systems kept by their own cellular programs. Nevertheless he also comes to the conclusion that emergence of life brings up a creative activity beyond computers.

3. Replication, mutation and negative selection acting on the hierarchy:

The basic formalism

$$d/dt \text{DNA}_{\text{vector}i} = \text{DNA}_{\text{vector}i} \times (r \times p(r)) \times (1-p(m)) \times (1-p(s)) \quad (\text{formalism 1})$$

is difficult to calculate in practice as r, m and s get inputs from all levels of the hierarchy 1-5, for instance regarding **replication**:

Level 1: Catalytic activity of nucleic acid

Level 2: enzymatic replication rate – note that here more detailed predictions are possible, e.g. using the results known for hyper-cycles (Eigen and Schuster, 1979; Emren et al., 2006).

Level 3: growth rate and cell cycle speed – note that here we and others made more detailed predictions using flux balance analysis for metabolic flow and including important regulatory effects from transcription factors (Eisenreich et al., 2006). A growth equation considering basic components critical for growth can be used to make solid and quantitative predictions for the growth rate under laboratory conditions (only one or no changing environmental condition, no direct competition etc.; Schuster et al., 2000; detailed example for methanogenic bacteria see Feist et al., 2006).

Level 4: Individual reproductive rate (including all sorts of detailed behaviour and mental abilities) – also for this accurate data and models are available from ecology, ignoring then the detail of the levels below (e.g. Nishida et al., 2003).

Level 5: Civilization growth rate (non-trivial to measure: BNP for example does not take into account environmental damages and long term sustainability). The basic formalism is simple but has to be extended here to rather complex socio-economic problems.

4. Mutation rate: This is composed of point mutations and more complex mutations (for instance gene duplications to acquire spare gene copies for new functions; this process is further enhanced by recessive genes in diploid organisms) as well as recombination in sexual species, in first simplification

Level 1: $p(m) = \text{direct mutation rate} \times \text{recombination rate} \times \text{recombination operator}$.

However, note that if we want to include even quantum effects then already the direct mutation rate alone is very complex to calculate, for instance regarding alkylating substances or UV effects on the DNA sequence.

Furthermore, in first simplification all higher levels diminish the mutation rate by different repair processes:

Level 2: diminish by enzymatic corrections (proof reading)

Level 3: diminish by cellular repair rate

Level 4: diminish by behavioural corrections such as mate selection

Level 5: diminish by social and medical corrections.

5. Negative Selection: Negative selection is used in formula 1 as it eliminates DNA from further generations. Its effect is most difficult to calculate. This is no accident: it results directly from the interactions of life with its environment which is again in an environment which is again ... and so on until the foundations of the world considered.

$p(\text{negative selection on level } i) =$

$p(\text{negative selection on level } i \text{ in small environmental context } j) \times$

$p(\text{negative selection on level } i \text{ in next bigger environmental context } j+1) \times$

$p(\text{negative selection on level } i \text{ in still bigger environmental context } j+2) \times \dots$

(Formalism 2)

One could propose that a certain, very big environment (e.g. a planet or a galaxy) is so huge that it could be considered outside from the context of the rest of the world. This is, however, logically not possible because any part of the universe which still is a part of our universe has to interact with the rest of it in some way (otherwise one could also define it as an independent further world).

However, even if somebody does not like this philosophical argument, it is clear from the start that for instance already the rate of detrimental point mutations depends from all kinds of radiation – including gamma rays from very distant quasars.

The total negative selection results from the negative selection possibilities on all levels i:

$$\begin{aligned} p(\text{negative selection}) &= p(\text{negative selection level 1}) \times p(\text{selection level 2}) \times \dots \\ p(\text{negative selection}) &= \prod_i (\text{negative selection on all levels } i) \end{aligned}$$

This has again to consider the open environmental context:

$$p(\text{negative selection}) = \prod_{i,j} (\text{negative selection on all levels } i \text{ considering all environments } j)$$

The formalism 2 is an infinite regress up to the Platon limit (or the boundary conditions of the most external environment). Interestingly, its renormalization (Cao and Schweber, 1993) in biology is effectively achieved by the limited storage of information available on each level (stochastic nature of mutations and limited amount of genetic or other information storage on the higher levels; Fig. S3a).

Implications (steps 6.-10.)

6. Simple implications for this set of features of life modelled:

- (i) Important properties of life can be formalized considering an increasing hierarchy of components encoded by a vector field of bit strings. These strings are storing information on their environment (useful for their survival) but also the higher levels of complexity encoded by them which then stores further types of information on the environment. The selection process depends on the environmental context which even for practical purposes is an iterative regress until the foundations of the world are reached. The context of the information stored is directly tested by survival and reproductive success.
- (ii) Life tends to be very flexible and it can be shown that in a competition situation in general the more flexible life type wins (selection for flexibility) and that this and other selection processes tend to increase selection pressure and speed up evolution (interspecies competition for instance) as well as the exploration of ever higher hierarchical levels (for example to improve homeostasis and evolutionary success). The starting level (nucleic acid evolution) can be described by a basic formalism. It is well compatible with formalisms for physical theories.

7. “Meaning” is introduced here in first approximation as meaningful behaviour (“ethics comes first”; see Taylor et al., 1998) and as a 4th level term of selection against bad (or non meaningful) behaviour (Fig. S3b). Surviving living beings have a behaviour that sustains survival, creativity and the potential to explore and grow, the universe in which they occur most probable mirrors these properties. Higher level terms (5th level etc.) refine this (ethics of a civilisation which does not kill itself by non-sustainability etc.; example: consensus and Kyoto agreement on carbon dioxide emissions, force for cooperative behaviour between people or even states).

Negative selection level 1: Quantum chemical inactivation of nucleic acid (in principle calculable but difficult). Furthermore, there exist elaborate algorithms to reconstruct evolution *a posteriori* from observed nucleic acid species diversity (e.g. phylogenetic reconstruction by neighbour joining, parsimony or, most accurate, maximum likelihood).

Negative selection level 2: Unstable / blocked hypercycle, depending on competition with other life (in particular polymerases and other nucleic acid templates; for this calculations are available, e.g. Emren et al., 2006)

Negative selection level 3: Cellular survival rate. Also here the competition in a real life ecosystem is extremely difficult to calculate. However, predictions of detrimental mutations and essential genetic information are possible for not too complex growth scenarios (e.g. Robubi et al., 2005, as well as work from many other molecular biology laboratories).

Negative selection level 4: Proper survival behaviour (which in real life situations include competition for limited resources and reproductive success; for this also literature is available, including to some extent at least energy considerations to summarize in a simple way the levels below; e.g. Iriarte et al., 2004; Nishida et al., 2003). Note that only at the multi-cellular level environmental selection leads to a simplified world model of an observer. In other words, already four levels of selection made sure that the basic concepts used for the behaviour are matching the real conditions in the environment. The genetic and further selection exerted by this allows for “synthetische Urteile a priori” (Kant) in such observers. Furthermore, only the complexity of this level (including the emergent phenomenon of an observer with conscience) allows to have the concept of “meaning” (whereas the concept of bit string and such a physical information content is already present at level 1).

Note that the bit string formalism applies also to other basic information storage devices in biological systems, apart from DNA e.g. RNA, PNA and more exotic storage types such as inheritance of membrane surface structures.

Negative selection level 5: Lack of sustainability and adaptability of a (technical) civilisation. Also very complex to calculate, empirically one can state that arthropod societies (ants, termites, bees) have far better stood the test of sustainability and survival during time then our comparatively novel human civilisation.

8. A formalism for complexity: Kolmogorov complexity (Schmidhuber, 2002) describes complexity of systems by the shortest program which can reproduce this complexity. We think this is not always a very reasonable definition. For instance, already the survival probability of a living DNA species (let alone life as a whole or our universe) is too complex to describe it shortly applying Kolmogorov complexity. To show this, we:

(i) first follow the argument by Chaitin (2006):

He showed that there are an infinite number of mathematical statements which can not be decided by a finite set of axioms. In particular, he investigated $O(N)$, defined as average probabilities for computer programs with a maximum length of N bits to stop. One can show that this number $O(N)$ can not be compressed, i.e. represented by a shorter program^{S1}. Moreover, an infinite set of such numbers $\{ O(N)_1, O(N)_2, O(N)_3, \dots \}$ even with infinite digits (general case) can be created which all can not be compressed (Chaitin, 2006, p.79).

(ii) We next consider that a DNA string with N bits has similar properties as such numbers of type $O(N)$. We regard the complexity for the probability of a DNA string to stop $O(\text{DNA})$ (regarding dying out, mutation, or its information processing probabilities): Its probability to stop, and the probability that a species dies out in general, can also only be described by a number $O(\text{DNA})$ as complex or even more complex then a number of type $O(N)$. There are several reasons for this, one is that the halting problem for any DNA based organism is more then Turing complex and NP complete^{S2}, furthermore we show above that the probabilities for mutation are in an infinite context (see formalism 2) and that both mutations and survival are stochastic processes, both add sufficient to the halting problem regarding a DNA and a species that its average stopping probabilities (or survival, mutation, information processing

probabilities etc.) only can be properly described by non compressible numbers $O(N)_{DNA}$ at least as complex as $O(N)$:

$$O(N)_{DNA} = O(DNA_{vector} \times (r \times p(r)) \times (1-p(m)) \times (1-p(\prod_{ii,ij} \text{selection all levels ii /envirnoment s ij})))$$

However, $O(N)$ numbers measure complexity resulting from averages over discrete, closed programs (or processes) which each are independent. In contrast, $O(N)_{DNA}$ numbers consider averages over open processes, interacting with an open (potentially unlimited) environment.

(iii) More to the point may thus be the following definition: Only the size of the slice of the total transition space (“omega”, the total space of all possible) should determine the degree of the complexity of an organism, environment/world or object/region of interest and used for comparisons. However, regarding biology the space and the slicing becomes a bit clearer:

Complexity is defined as the number of structuring information units (in biology: replicating species; in physics natural laws, in general further structure defining parameters) and hierarchies used as well as their individual information content.

To cast this into a formalism describing the complexity of an object or even a world (Fig. 2S; Table 1S), the number of all contained Kolmogorov processes K is compactly described by a program $C(K)$ with length l , and we collect all non-compressible phenomena from the type of $O(N)$ numbers (process averages, stopping probabilities etc.) as well as all more complex interacting non-compressible phenomena such as life ($O(DNA)$ numbers e.g. species, DNAs, etc.)

$$\text{Complexity (object)} = \text{length } (C(K)) + \{ O(N)_1, O(N)_2, \dots \} + \{ O(DNA)_1, O(DNA)_2, \dots \}$$

(Formalism 3)

As Chaitin (2006) already pointed out (and Cantor earlier, see Kanamori, 1996), in general this implies comparing very high up to infinite sets of non-compressible numbers if we want to compare the complexity of objects and in particular the complexity of different worlds (with their variations in their laws of physics). However, this can be done with set theory even for infinite sets and their cardinality. Furthermore, this supports the conjecture that with very high probability an observer is situated not only in a world that is complex^{S3} but that in fact the most complex world has by far the biggest slice of all states.

This is very well applicable to life (nn DNA species and five or more layers of hierarchy which each contain a large amount of information due to their individual components).

The definition is also applicable to physical objects. A large planet covered just by methane ice would for example be much less complex then the earth as the main structuring information of this simple planet would just be gravity and the chemistry of the methane ice (Fig. S1; details Table 1S).

We stress that this is only a first operational definition to quickly identify and describe complexity in very different system. In contrast, further details of a stringent definition of complexity are – no wonder – very complex and difficult to capture, in particular as we showed that Kolmogorov complexity (Schmidhuber, 2002) is not enough for complex phenomena such as life or a universe with life. As one aspect this implies that creativity (see above) requires a hierarchy, building blocks, emergent system behaviour and variation potential (Fig. 1). This includes targeted variation (level 4 and 5): Individual creative expression requiring an individual mind or person. In a very first approximation (as creativity is also Kolmogorov non compressible!), structuring information units (enzymes etc.) together

with randomness, systems behaviour and channelling lead generally to creative behaviour – in a favourable, sufficiently complex universe^{S3}.

Notes:

^{S1}Proof sketch (see also Chaitin, 2006, p. 80): The strategy for demonstrating that omega is incompressible is to show that having the first N bits of omega would tell me how to solve the Turing halting problem for programs up to length N bits. It follows from that conclusion that no program shorter than N bits can compute the first N bits of omega. (If such a program existed, I could use it to compute the first N bits of omega and then use those bits to solve Turing's problem up to N bits—a task that is impossible for such a short program.)

^{S2}Csuhaj-Varju E, Freund R, Kari L, Paun G. DNA computing based on splicing: universality results. Pac Symp Biocomput. 1996;:179-90.

^{S3}We suggest that to exist in an escalating complex universe is sufficient to have phenomena such as life. Note that elementary states (nodes) and interactions between them (edges) can quickly become rather complex even with a comparatively limited number of elementary states if the escalating property holds and interactions of interactions (as super-nodes) are iteratively possible. As with recursive functions in general (e.g. Ackermann function) such a state space becomes quickly very large. One further level of recursion more leads to an excessive larger state space, hence the most complex world probably owns the largest slice of the complete state space (Fig. 3 in the paper).

Further extensions (however, more speculative)

8. (iv) If already survival probabilities for any DNA species are non compressible complex (and there are many more and similar other types of phenomena of this complexity) it is clear that our universe is even more difficult to capture, there will be no simple cellular automaton program (as hoped for by Wolfram, 2002) to capture its complexity or any shorter Kolomogorov type of program. The non-compressible nature of our universe suggested here argues against a singularity at Big Bang (how should the singularity store sufficient information - in particular as we showed above that no simple Kolmogorov type of program or simple laws will do the trick) and is well in line with recent results on the quantum nature of the Big Bang (Ashtekar et al., 2006).

Our definition stresses emergent phenomena (including new hierarchies) and any type of new or additional representation and information storage adds to the complexity even if the object investigated is already non compressible complex by a Kolmogorov-type of definition. However, if you have phenomena such as life you are at least for sure in a Kolomogorov-non compressible complex universe. We speculate that the most complex universe takes an excessive large slice of the complete state space (Table 2S; see also below). Alternatively, one could also argue that any type of an escalating complex universe (for a given set of physical parameters and so fine tuned that it becomes escalating complex including permissive for life) is only a flavour or variant of the same complex universe (very much - and this is no accident - as the different flavours of String Theory are all variants of the M-theory). According to our hypothesis, only in the fine-tuned parameter sub-space which is permissive for life an observer exists, the many alternative physics and worlds compatible with String Theory are without life and inherently less complex than this sub-space.

9. Examine instead of a naïve “theory of everything” (TOE) a framework relying on transition probabilities:

Fundamental: To derive a common framework relevant for physics and biology, we start and assume chaos to be the general and basic state. In chaos nothing is restricted or defined and all is possible. Active pattern generation is thus necessary to have even something as simple as similar elementary particles. We thus have in any world random processes (chaos) vs. guided processes (natural laws, fields, replicating species). This dichotomy yields the differences in complexity, comparing different environments, worlds and “universes”. Random worlds are simple. More complex worlds or universes have more and distinguishable guided processes. You compare and count the number of self generating processes in each world (Fig. S1):

A1) A quantum spin loop field generates space and time.

A2) Natural laws generate similar particles (this can be cast into an operational tool working on the quantum spin loop field. This then generates particles and fields in a space time etc.)

B) On a qualitatively new level, biology store information and uses it for self generating species.

Note that we can only show here some interesting parallels between physics and biology in such a framework, a closed or complete TOE is naïve for any field, even for mathematics (Chaitin, 2006). Moreover, see also the points from Rovelli (2004), where he is suggesting for physics rather independent formalisms (quantum spin-loop theory etc.) then expecting a unified and complete TOE of physics as sometimes hoped for from String Theory. Similarly, a number of holistic approaches covering physics and biology including the process of observation have been proposed by physicists (e.g. by Erwin Schrödinger, Werner Heisenberg, David Bohm, Roger Penrose, Lee Smolin – as well as more esoteric ones, e.g. by Fridjoff Kapra). These have all their merits and specific perspectives as well as limitations but are not discussed further here. As an alternative perspective, we start here not from

physics but the framework focus is to include basic properties of life and its internal representation of information.

Combined description: A transition state formalism is well suited here as we want to describe the complete state space accessible both for physical objects as for objects from biology. A key is pattern self generation against the random chaos. This occurs from a) pure patterns from a standard physical law (a “platonic” law), b) by biology, c) other self generation processes. Thus we can combine the following formalisms for a combined biological and physical description of the world (and only in this sense a theory of everything):

A TOE from physics would start from the standard model of physics (see e.g. Griffiths, 1987; Barrow, 1991; Rovelli, 2004) and include formalisms such as (Rovelli, 2004):

- (i) Salam Weinberg formalism
- (ii) Yang-Mills field
- (iii) Ashtekar formalism (integrating (i) and (ii)), i.e. the physical transition probabilities which describe the evolution of a spin network. For a spinfoam σ bounded by the spin networks s and s' this yields the formalism (Rovelli, 2004)

$$W(s, s') \sim \sum \mu(\sigma) \prod A_v(\sigma)$$

Here A_v is the vertex amplitude and $\mu(s)$ is a measure term. The sum is over the whole spin foam and the product over all vertices. The spin foam formalism allows to construct a background free and in this sense comprehensive physics. Moreover, for this there are interesting parallels with biology (see below). However, there are several solid alternative candidate theories to push the standard model further to include gravitation, for instance string theory (Green, 2000) as well as various alternative suggestions (e.g. Niedermaier, 2006).

For our framework we now add DNA transition probabilities and the probability of extended information storing processing hierarchies:

- (iv) $d/dt \text{DNA}_{\text{vector}i} = \text{DNA}_{\text{vector}i} \times (r \times p(r)) \times (1-p(m)) \times (1-p(s))$ (formalism 1)
- (v) n-level hierarchy (extended n-dimensional arrays of $\text{DNA}_{\text{vector}nm}$ for new levels of information storage and components encoded by the lower levels; biological experience of “meaning” is contained from level 4 onwards)

Thus we add here standard formalisms of physics (i), (ii) or a well known example for current new formalisms in physics (iii) to a more complete description of the world but have independent formalisms for biology (iv, v).

However, we can next derive a formalism from (iii), (iv) without time (“background free”, Rovelli, 2004) with respect to the highly dimensional fitness landscape of evolution, depending on all species present and all possible mutation, replication and selection rates. This is not elaborated here, but this integrates (iii) to (v) into a common mathematical framework. As in the spin foam formalism (iii) above one can construct a DNA spin network, nodes (“particles”, Rovelli, 2004) represent then DNA populations and edges (“forces”, Rovelli, 2004) represent then kinetic DNA vectors of increase or decrease in the species, $d/dt \text{DNA}_{\text{vector}i}$. Furthermore, we would again describe probabilities of states and species in a background free form and trace the complete space of transitions accessible. This sketch is at least promising and applying a common, background free description and an abstract state space both to basic biological and physics entities.

For certain simple biological systems direct results have already been calculated in such evolutionary fitness landscapes, e.g. for RNA species first with no switches (“neutral path”) and subsequently studying clear switches in their structure and function by mutation (e.g. Reidys et al., 2001). This evolutionary landscape is of course on a far higher system level than the basic spin foam (Fig. S3c).

10. Observation: Another implication from our theory on internal representation of information in biological systems concerns the process of observation. In particular, there is the problem (Penrose 1990, 1996) how the clear defined state R of a macroscopic measurement (“an observation made by an observer”) arises from the undefined or multiple open states of the quantum wave function U is explained in the context of this theory as resulting from several physical and biological selection processes building up the hierarchy up to the macroscopic observer and is thus much more economical (or, in fact, less “ad hoc”) than Everett-like models (of constant splitting worlds with each measurement; Seligman et al., 1973; see box E):

a) For a given observer there is only one world with a large number of microstates. The defined measurement is only there for the past and selected from the microstates accessible from a present state of the observer by the arrow of entropy (this would break down if there is no steep and clear entropy gradient). A defined trajectory and clear, continuous world line results (the future is undefined for the same reason, many accessible states are there). b) Macroscopic states (observer and macroscopic observation), are already the result from a selection process of several hierarchies (e.g. all de facto realized DNA representatives of a species and accordingly for each other level of complexity). c) In a background free model (Rovelli, 2004) or at least a description without time it becomes even clearer that in general only a limited number of macroscopic states such as an observer having a certain state including an observed measurement (or, one level higher, all in this world evolutionary accessible representatives of a species) is resulting from the much higher but again limited number of elementary microscopic states and their interactions and selection on higher levels. Different observational trajectories are possible taking all observers together which are realized by selection from the microstates and their interactions (Fig. S3c). The microstates form a web (Fig. S3c): From one state there are always several other ones accessible, there are no “hidden variables” to discriminate between them, the web gives for any state in general several possibilities (in general with different weights) to access several other states. In contrast selection at the higher levels of complexity⁵³ and the arrow of entropy lead to only a much lower number of macroscopic states including observers and their macroscopic observations. Moreover, for any observer there is a clear, unique and continuous world line of states with increasing entropy as measurements can only be made if the entropy increases (Fig. S3c).

An observer searches “meaning” in his environment (“The answer to life, the universe and all the rest...”):

The “meaning” of this complex universe is an observer dependent look at a particular slice (a “world”) of the Platon space of all possible. Formalism 1 allows to calculate (given specific initial conditions ranging from the number of DNA species involved, enzymatic replicases, transcription factors and cellular networks to neuronal architecture) the reflected world model of an organism. This works for instance sufficiently accurate in *C.elegans* genetic networks where occurrence of individual neurons can even be accurately predicted (Schade et al., 2004). This is a comparatively simple model neural organism, thus simple animal behaviour and “meaning” is found here (avoiding and appetite behaviour, for example; Fig. S3b).

More complex organisms such as human beings have more refined concepts of “meaning”. This concept of “meaning” is already beyond formal systems and the Gödel limit (Fig. 2) and of course, also NP-complete.

Such observers are only a minor part of their world. Hence, the complexity of the world is even more beyond the Gödel limit or the Turing calculability. In fact, most probable we are in the most escalating complex universe (details in Table 2S).

Platon space of all possible. in the spirit of Platonic philosophy (Kirk et al., 1983) and similar to Cantor’s creation (Kanamori, 1996) of all sets and cardinal numbers from the empty set, an environment and its specific existence (or more ambitious cosmological world existence, “creation”) can also be investigated. Formalism 2 already shows that iterating the environment of the environment ultimately leads to the “Platon limit”: The foundations of the world. This is no very large physical space; rather physical space is one of the properties a world can have. In general, a world can have many properties, however these properties can either be very well defined (e.g. in our world the nature constants such as the charge of the electron, the gravity constant, Planck’s constant) or exist over a broad range (e.g. space, time, energy etc.). The fundament of any world is thus the “Platon space” of all properties or *the space of all possible environmental properties (“platonic ideas”)*. To give rise to a world, several properties have to combine, with preference some well defined ones and some with a broad range of values (as in our world with its specific parameter settings of physical laws). Properties are not forced to combine, but pure properties do not yield a complete environment (“pure ideas do not yield a world”), only combinations between properties do (for our world a central property is to have mass, postulated to be mediated by the Higgs-boson; Barrow, 1991). The space of all abstract properties (“Platonic ideas”) includes also all such combinations (“worlds”) as well as their pure states (“pure ideas”).

This is a more refined explanation of the “space of all possibilities”. Our real foundations are basic environmental / world properties (“Platonic ideas”). Our more mundane everyday ideas are simply a faint shadow of these (“Höhlengleichnis” of Plato). The escalating property of life (formalism 1) is in this sense also a transcendent principle if we include life in this way in a theory framework (step 9). A living observer can identify meaning in his world. In particular we see that interpretation of a certain meaning requires life, however each biological meaning was already selected by the world and its foundations.

Box E. Observer and observation (speculative model). Everett (1957) was the first to suggest that quantum uncertainty implied the existence of many worlds (multiverse) differing only in the realized quantum states (Seligman et al., 1973). However, in its general version the Everett model implies that for each choice we (as macroscopic observers) or an elementary particle can make, there should then exist a parallel world(s) where the alternative quantum state(s) are realized. This postulates an exponential increase of worlds for every quantum state with alternatives. Occam’s razor suggests that simpler models should be preferred if they explain all observations similar well and a model of the world where constants “splits” into parallel worlds occur is also not very convincing regarding for instance the splitting process itself. A number of modified Everett models have been proposed earlier, for instance stressing decoherence, and a number of models rejecting Everett models exist (see for both e.g. Tegmark, 2007). The following model adds to these from our biology motivated background free description of macroscopic states such as life (see formalism 1; Suppl. Material including step 9). Our model (Fig. S3c) suggests only one world based on a web of quantum spin-loop states, a limited number of macroscopic states for the observer (and no splitting new worlds) and each observer has a limited horizon of observation (on his time trajectory).

1. Elementary quantum states (“microstates”) have transition probabilities to several other states. The model uses for this the quantum spin foam formalism:

$$W(s,s') \sim \sum \mu(\sigma) \prod A_v(\sigma)$$

Here A_v is the vertex amplitude and $\mu(s)$ is a measure term. The sum is over the whole spin foam and the product over all vertices. The spin foam formalism allows to construct a background free and in this sense comprehensive physics. Furthermore it is from the start clear that this model exists without a specific time coordinate, rather the elementary states are connected with each other, and in general from one state there are transitions to several other states. The spin foam forms a web with many possibilities from each node to continue. However, there is only one world and one web, no splitting of worlds what so ever (Fig. S3c).

2. “Time” is in our model only possible if entropy can be measured and thus applies only to any type of larger (“macroscopic”) ensemble (recognizable macroscopic entities be it human beings, planets or any other type of object). For such an ensemble of microstates entropy can be measured. The transition probabilities for the microstates are given by the spin foam. However, for the macroscopic ensemble there are many states available with increasing entropy (“future”) and very few (on the macroscopic level often only one) with lower entropy (“past”). Macroscopic states which do quantum physics (“observers”) will see that the microscopic states exhibit a web of transition states.

3. However, also the macroscopic states can be described background free (similar to the spin foam) without time. No “splitting” of worlds occurs in this model, rather for a given macroscopic ensemble (e.g. a human observer) with a certain degree of entropy only a limited number of states (maybe high) exist (Fig. 3Sc). This applies for all degrees of entropy as long as compatible with life. This is a clear upper limit for the number of these macroscopic states, further, different hierarchies of selection (including system stability and biological evolution) make sure that many of these are not possible. Furthermore, of the remaining many are never reached by evolution due to a number of reasons such as building block limitations (Hartl, 2007; Gould, 1997) or as they are not reachable by an evolutionary path with positive fitness (Weinreich et al., 2006).

4. This leaves a reduced and limited number of macroscopic states for the living observer with a given level of entropy. The time trajectories possible to experience observations for these observer states are also limited and given by the arrow of entropy but are potentially more (as from each state of the observer with a given entropy there are several states with lower entropy reachable). However, these different “futures” do also partly overlap (having only slightly different microstates in the observer leads in fact often to a large overlap of the next reachable macroscopic observer states). Moreover, the number of time trajectories which can be experienced or observed does not add anything to the fixed number of states with a given entropy an observer can only have.

This is of course only another attractive and different model to the typical model of many worlds for each observation suggested by Everett type models (Seligman et al., 1973; Buchanan, 2007; Tegmark, 2007). Furthermore it certainly does not rule out other reasons to consider multiverses (e.g. eternal inflation according to Linde, 1982 and later works) or, as done throughout here, the general richness of physical parameter settings which would yield very different “worlds” and observers.

Alphabetical reference list for supplementary material (including all references)

- Adams, D. *The hitchhiker's guide to the galaxy*. Ballantine Books (ISBN: 0345391802). Del Rey; Reissue edition (1995)
- Almaas E, Kovacs B, Vicsek T, Oltvai ZN, Barabasi AL. (2004) Global organization of metabolic fluxes in the bacterium *Escherichia coli*. 427(6977):839-43.
- Alvarez-Vasquez F, Sims KJ, Cowart LA, Okamoto Y, Voit EO, Hannun YA. Simulation and validation of modelled sphingolipid metabolism in *Saccharomyces cerevisiae*. *Nature*. 2005 Jan 27;433(7024):425-30.
- Ashtekar,A., Pawlowski,T., Singh,P. (2006) Quantum nature of the Big Bang. *Phys.Rev.Lett.* 96 (2006) 141301
- Ball, P. Is physics watching over us? *Nature Science update*, 13th Aug. (2002)
- Barrow, J. D. *Theories of Everything*. Oxford Univ. Press (1991).
- Barrow, J. D. *The Constants of Nature*, Pantheon Books, [ISBN 0375422218](#) (2003).
- Bi G, Poo M. (1999) Distributed synaptic modification in neural networks induced by patterned stimulation. *Nature*. 1999 Oct 21;401(6755):792-6.
- Bork P, Jensen LJ, von Mering C, Ramani AK, Lee I, Marcotte EM. Protein interaction networks from yeast to human. *Curr Opin Struct Biol*. 2004 Jun;14(3):292-9.
- Buchanan,M. See me here, see me there. *Nature* **448**, 15-17 (2007).
- Cao, Tian Yu and Schweber, Silvan S. (1993) The Conceptual Foundations and Philosophical Aspects of Renormalization Theory, *Synthese*, 97(1), 33-108.
- Carr, B .J. & Rees, M. J. The Anthropic Principle and the Structure of the Physical World. *Nature* **278**, 605-612 (1979).
- Chaitin, G. The limits of reason. *Sci Am.* **294**, 74-81 (2006).
- Chapline, G. *Dark energy stars*. Texas conference on relativistic astrophysics, Stanford, CA, 12/12/2004-12/17/04 (2004).
- Cooper; J.M. (ed.), *Plato: Complete Works*. Indianapolis/Cambridge: Hackett Publishing Co. Inc. 1997
- Ditfurth, H. v. *Wir sind nicht nur von dieser Welt* (10th edition 1994) Deutscher Taschenbuch Publ., München (1984).
- Emren LO, Kurtovic S, Runarsdottir A, Larsson AK, Mannervik B. From the Cover: Functionally diverging molecular quasi-species evolve by crossing two enzymes. *Proc Natl Acad Sci U S A*. 2006 Jul 18;103(29):10866-70. Epub 2006 Jul 7.
- Eigen,M., Schuster, P. (1979) *The Hypercycle - A Principle of Natural Self-Organization*, Springer-Verlag, Berlin.
- Eisenreich W, Slaghuis J, Laupitz R, Bussemer J, Stritzker J, Schwarz C, Schwarz R, Dandekar T, Goebel W, Bacher A. (2006) 13C isotopologue perturbation studies of *Listeria monocytogenes* carbon metabolism and its modulation by the virulence regulator PrfA. *Proc Natl Acad Sci U S A*. 103(7):2040-5. Epub 2006 Feb 6.
- Everett, Hugh (1957) Relative State Formulation of Quantum Mechanics. *Reviews of Modern Physics* vol 29, 454-462.
- Feist AM, Scholten JC, Palsson BO, Brockman FJ, Ideker T. Modeling methanogenesis with a genome-scale metabolic reconstruction of *Methanosarcina barkeri*. *Mol Syst Biol*. 2006;2:2006.0004. Epub 2006 Jan 31.
- Felder, K. (1996) Kenny's overview of Hofstadter's explanation of Gödel's Theorem. <http://www.ncsu.edu/felder-public/kenny/papers/godel.html>.
- Gott, J. R. III. Implications of the Copernican Principle for Our Future Prospects. *Nature*, **363**, 315 (1993).
- Gould SJ. The exaptive excellence of spandrels as a term and prototype. *Proc Natl Acad Sci U S A*. 1997 Sep 30;94(20):10750-5.

- Green, B. *The Elegant Universe: Superstrings, Hidden Dimensions, and the Quest for the Ultimate Theory*. Vintage Publ. (Bertelsmann), New York, ISBN 0375708111 (2000).
- Griffiths, David J. *Introduction to Elementary Particles*. Wiley, John & Sons, Inc. ISBN 0471603864 (1987).
- Hartl D. The spandrels of the genome. *Nat Genet.* 2007 Jul;39(7):811.
- Hofstadter, D. R. *Gödel, Escher, Bach: an Eternal Golden Braid*. Basic Books; Jackson, TN (1979).
- Igamberdiev AU (2006) Physical limits of computation and emergence of life. *Biosystems.* 2006 Sep 24; [Epub ahead of print]
- Iriarte J, Holst I, Marozzi O, Listopad C, Alonso E, Rinderknecht A, Montana J. (2004) Evidence for cultivar adoption and emerging complexity during the mid-Holocene in the La Plata basin. *Nature* 432(7017):614-617.
- Kanamori, A. (1996) The mathematical development of set theory from Cantor to Cohen, *Bull. Symbolic Logic* 2, 1-71.
- Koonin, E. The cosmological model of eternal inflation and the transition from chance to biological evolution in the history of life. *Biol Direct.* 2, 15 (2007).
- Kirk, G.S., Raven, J.E. & Schofield, M. *The Presocratic Philosophers* (2nd Ed.), Cambridge University Press (1983).
- Linde, A.D. (1982) A new inflationary Universe, *Phys. Lett.* B108, 389.
- Monod, J. *Chance and Necessity*. New York. Vintage paperback ISBN 0394718259 (1971).
- Mukherji, M., Bell, R., Supekova, L., Wang, Y., Orth, A. P., Batalov S, Miraglia L, Huesken D, Lange J, Martin C, Sahasrabudhe S, Reinhardt M, Natt F, Hall J, Mickanin C, Labow M, Chanda SK, Cho CY & Schultz PG. Genome-wide functional analysis of human cell-cycle regulators. *Proc Natl Acad Sci USA* 103, 14819-14824 (2006).
- Niedermaier, M. (2006) The asymptotic safe scenario in quantum gravity. Gr-qc/0610018 <http://arxiv.org/abs/gr-qc/0610018> (preprint server)
- Nishida T, Corp N, Hamai M, Hasegawa T, Hiraiwa-Hasegawa M, Hosaka K, Hunt KD, Itoh N, Kawanaka K, Matsumoto-Oda A, Mitani JC, Nakamura M, Norikoshi K, Sakamaki T, Turner L, Uehara S, Zamma K. Demography, female life history, and reproductive profiles among the chimpanzees of Mahale. *Am J Primatol.* 2003 Mar;59(3):99-121.
- Penrose, R. *The Emperor's New Mind*, Oxford University Press (1990).
- Penrose, R. *Shadows of the Mind: A Search for the Missing Science of Consciousness*. Oxford University Press; Reprint edition (1996)
- Pretement, S. In: *The dictionary of the History of ideas*. The electronic text Center, University of Virginia Library. Gale Group, Charlottesville, VA. <http://etext.lib.virginia.edu/cgi-local/DHI/dhi.cgi?id=dv2-05> (2003).
- Reidys C, Forst CV, Schuster P. (2001) Replication and mutation on neutral networks. *Bull Math Biol.* 2001 Jan;63(1):57-94.
- Robubi, A., Müller, T., Fueller, J., Hekman, M., Rapp, U. & Dandekar, T. c B-Raf and C-Raf signaling investigated in a simplified model of the mitogenic kinase cascade. *Biol Chem.* 386, 1165-1171 (2006).
- Rovelli, Carlo (2004) *Quantum Gravity*. Cambridge University Press.
- Sasagawa S., Ozaki Y., Fujita K., Kuroda S. (2005) Prediction and validation of the distinct dynamics of transient and sustained ERK activation. *Nat. Cell Biol.* 7, 365-373.
- Schade MA, Reynolds NK, Dollins CM, Miller KG. Mutations that rescue the paralysis of *Caenorhabditis elegans* ric-8 (synembryon) mutants activate the G alpha(s) pathway and define a third major branch of the synaptic signaling network. *Genetics.* 2005 Feb;169(2):631-49. Epub 2004 Oct 16.
- Schmidhuber, J. Hierarchies of generalized Kolmogorov complexities and nonenumerable universal measures computable in the limit. *International Journal of Foundations of Computer Science* 13(4):587-612 (2002).

- Schuster S, Fell DA, Dandekar T. (2000) A general definition of metabolic pathways useful for systematic organization and analysis of complex metabolic networks. *Nature Biotechnol.* 18(3):326-32.
- Seligman, B., DeWitt, R., Graham N. (eds.) *The Many-Worlds Interpretation of Quantum Mechanics*, Princeton Series in Physics, Princeton University Press (1973), ISBN 0-691-08131-X
- Shamovsky I, Ivannikov M, Kandel ES, Gershon D, Nudler E. RNA-mediated response to heat shock in mammalian cells. *Nature*. 2006 Mar 23;440(7083):556-60.
- Smolin, L. *The Life of the Cosmos*. Oxford University Press (1997).
- Suel, G. M., Garcia-Ojalvo J., Liberman, L.M. & Elowitz, M. B. An excitable gene regulatory circuit induces transient cellular differentiation. *Nature* **440**, 545-550 (2006).
- Taylor, C.C.W., Hare, R.M. & Barnes, J. *Greek Philosophers — Socrates, Plato, and Aristotle*, Oxford University Press, NY (1998).
- Tegmark, M. Many lives in many worlds. *Nature* **448**, 23-24 (2007).
- Thakar, J., Schleinkofer, K., Borner, C. & Dandekar, T. RIP death domain structural interactions implicated in TNF-mediated proliferation and survival. *Prot. Struc. Func and Bioinf.*, **63**, 413-423 (2006).
- Ubersax, J. A., Woodbury, E. L., Quang, P.N. , Paraz, M., Blethrow, J. D., Shah, K. , Shokat, K.M. & Morgan, D.O. Targets of the cyclin-dependent kinase Cdk1. *Nature* **25**, 859 (2003).
- Uexkuell, J. v. & Kriszat, G. *Streifzüge durch die Umwelten von Tieren und Menschen. Ein Bilderbuch unsichtbarer Welten*. Berlin (1934) [Uexküll / Kriszat 1956: 136f.]. Figge, Udo L.: 'Jakob von Uexküll: Merkmale and Wirkmale', in: *Semiotica* **134**, 193-200 (2001).
- Vastrik, I., D'Eustachio, P, Schmidt, E., Joshi-Tope, G., Gopinath, G., Croft, D., de Bono B, Gillespie M, Jassal B, Lewis, S, Matthews, L, Wu, G., Birney, E. & Stein L. Reactome: a knowledge base of biologic pathways and processes. *Genome Biol.* **8**, R39 (2007).
- Weinreich DM, Delaney NF, Depristo MA, Hartl DL. Darwinian evolution can follow only very few mutational paths to fitter proteins. *Science*. 2006 Apr 7;312(5770):111-4.
- Wolfram, Stephen (2002) "A New Kind of Science" Wolfram Media Inc. Champaign Illinois. [ISBN 1-57955-008-8](https://www.wolfram.com/bk/new-kind-of-science/)

Supplementary Figures

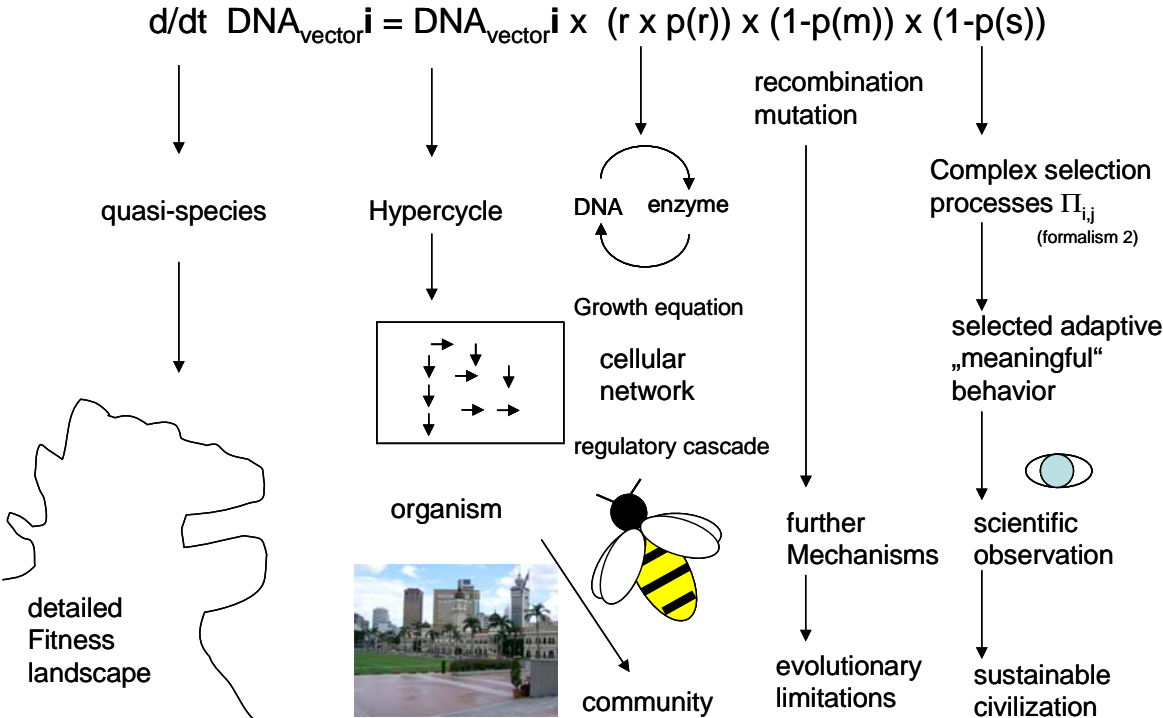


Fig. S1. A formalism for key processes of life. Our approach uses one basic concept and formalism (formalism 1; stochastic transition probabilities; see also Fig. S3c) which is known from physics but can be also very clearly implemented for the description of survival of DNA species and any more complex biological system. Different hierarchical levels are illustrated and can be considered such as quasi-species, evolutionary fitness landscapes, metabolic fluxes, genetic networks and ecological competition. For these exact calculations have been derived and experimentally verified (see text). All these levels are integrated by the formalisms given.

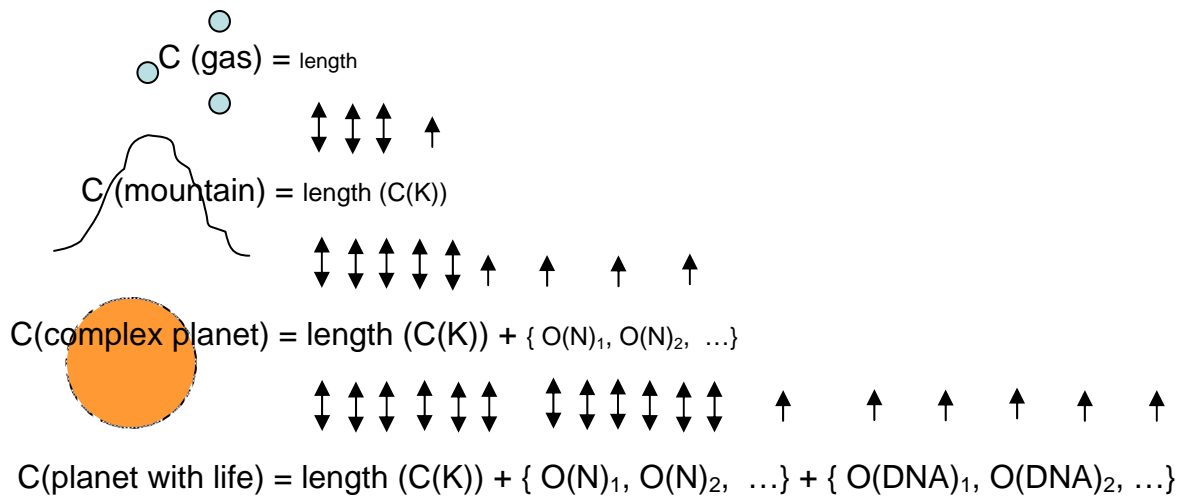


Fig. S2. Measuring complexity in different objects. A complexity measure is in general challenging and difficult to give (reviewed in Schmidhuber, 2002). Here we examine a measure which analyzes a complex object by summing up those parts which can be replicated by a shorter program (Kolmogorov complexity $C(K)$) and next considers and counts all non-compressible phenomena in the object. These are either those which are similar complex as $O(N)$ numbers (Chaitin complexity averaging over separated processes) plus those aspects of the object which are even more complex ($O(\text{DNA})$ numbers; interconnected processes in an open and potential infinite environment). Detailed comparisons for simple (a gas), large (a mountain, a planet) up to infinite complex objects (a world with life) are possible applying set theory (symbolized by arrows with partner elements or without). The error from simplification or simplified descriptions of the object can furthermore be quantified by the formalism even for non-compressible complex phenomena including life.

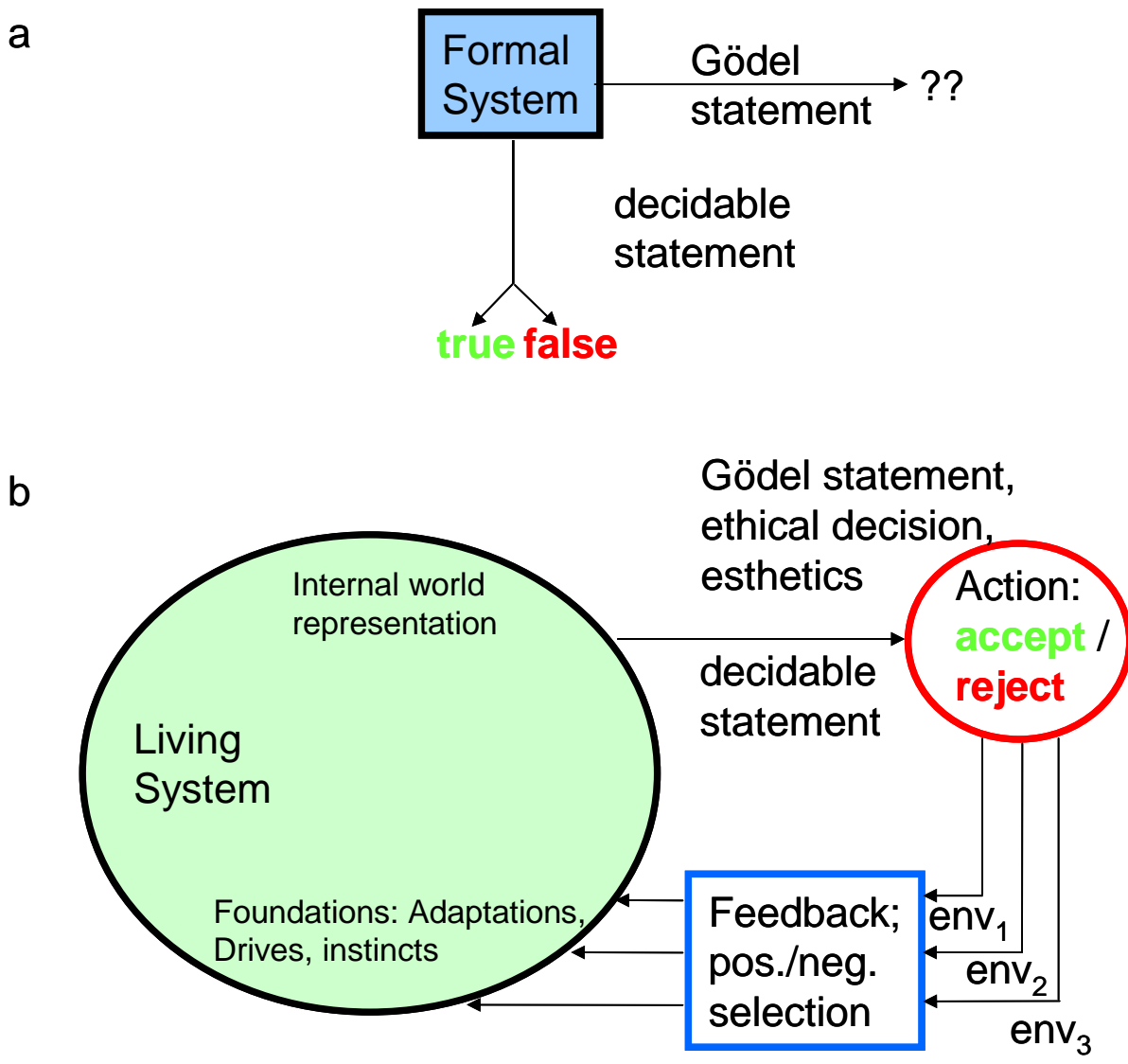


Fig. S3a. Answers to fundamental questions: Unpredictable strategic decisions in an infinite context. Living observers can answer fundamental questions which can not be decided by formal systems (e.g. solve and reflect on mathematical paradoxes, but even more so on non-compressible complex questions such as aesthetics, ethics, freedom and arts). Living beings as open systems selected and surviving in an infinite context of ever larger environments are ideally geared for this. Decisions are not made by formal logic of a closed system (“true” / “false” statement; top) but according to survival heuristics and selected adaptation strategies for the complex world the organism has to survive in (“reject” / “accept” a certain action to the statement; bottom). Fundamental decisions are and can be made by the observer in a limited time, with defined decision state but unpredictable (and stochastic) outcome.

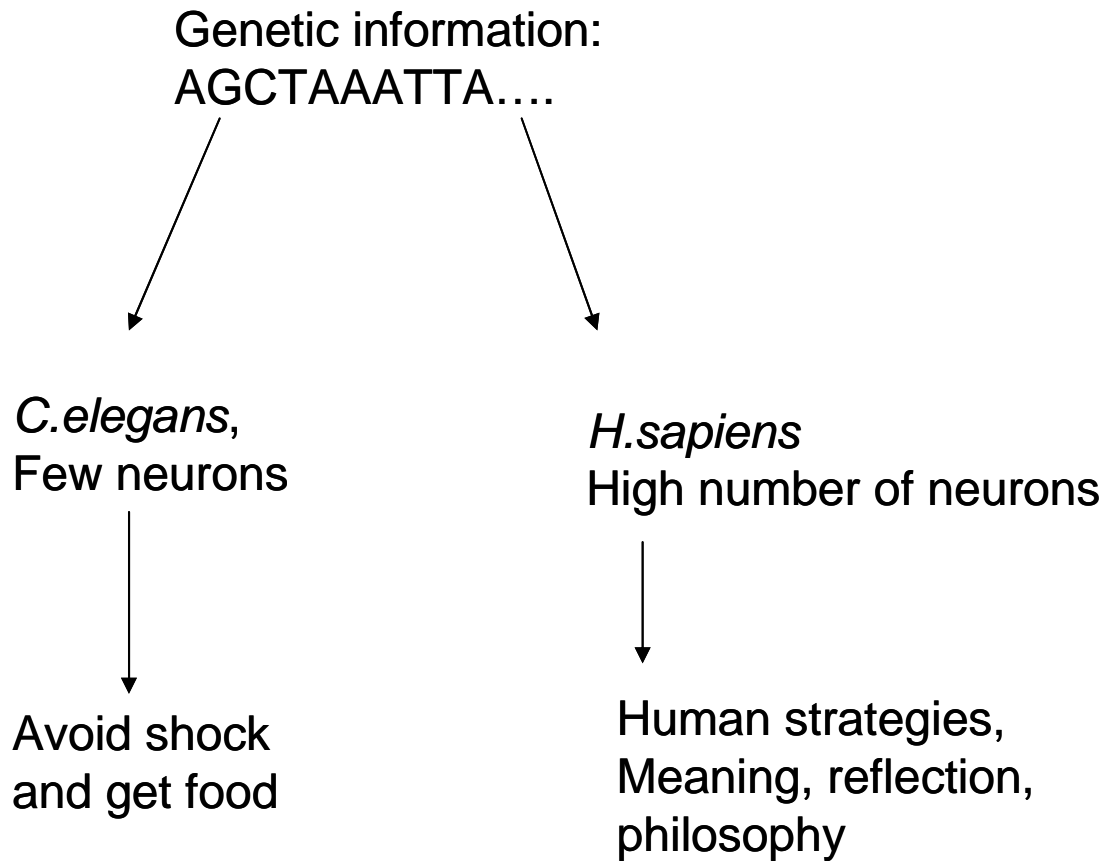


Fig. S3b. “Meaning” arises as a system effect. The biological concept of “meaning” arises in an observer from active and inherent system drives and his world- and self-representation. This requires many neurons, learning and individual memory, DNA and genetic memory is not sufficient. It is thus part of the self generating internal information storage typical for life if levels beyond DNA storage (top) are considered. In humans (right) this includes higher meaning, reflection and philosophy. As in the cell cycle example, ethical dilemmas or other fundamental problems may be formally undecidable from within the system / the observer. However, a living being would nevertheless decide stochastically in such a way that they maximize on average their long term survival. “Meaning” depends on the observer, including the “meaning of the universe” (there are more than enough meaningful and inspiring features in an exceedingly complex universe for any living observer; Fig. 3).

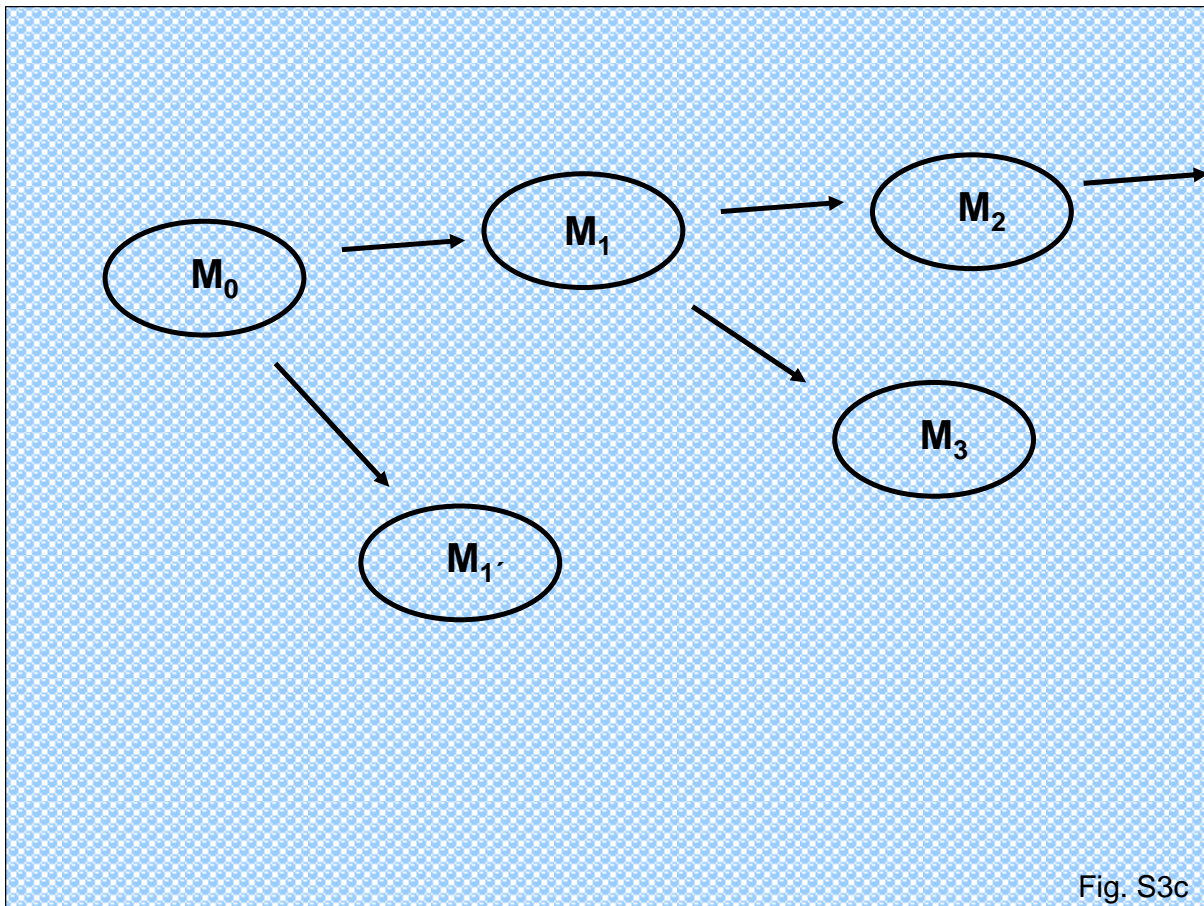


Fig. S3c

Fig. S3c. Defined observations from a web of elementary states. Microstates (blue balls) are undividable elementary states (quantum states, quanta, e.g. quarks). Macrostates M are ensembles of microstates. “Worlds” W are certain parameter settings of state space properties. Our theory allows a background free (without time, space) description of life, observer and observation (positioned in the context of the abstract evolutionary fitness landscape). It interprets defined observations and measurements (classical, R or real, defined states; Penrose, 1990) only arising from the selection processes on all levels of the hierarchy from elementary processes to the observer. The fundamental elementary processes stay as wave functions, undefined (U) in multiple states: The elementary states form an open, background-free quantum-spin-loop web (blue balls in background) and any node is connected stronger or weaker (different quantum probabilities) to different alternative states. Macroscopic states M such as observers with a certain observation (M_0 to M_3) are special, fewer and arise only after different selection processes happened on several higher hierarchical levels. “Time” arises in this background free description only in the observer (e.g. in state M_1) as the arrow of entropy allows to identify clearly the earlier observation state with lower entropy (M_0), the future is unclear as there are many possibilities to increase entropy (M_3 or M_2). An alternative macroscopic state with similar entropy (M_1') may exist but can not be directly observed from M_1 . There are no hidden variables. This theory is in this respect much clearer, more economical (much lower number of elementary states and macroscopic states postulated) and defined than a number of alternatives (e.g. by Penrose, Everett or Bohm). In particular, a typical Everett-like model (see Seligman, 1973; Tegmark, 2007) requires constant splits of “worlds” whereas Fig. S3c illustrates that only microscopic states form a web (blue balls, Fig. S3c). The numbers of trajectories between the much fewer macroscopic states are much fewer, the arrow of entropy imposes additional restrictions on the number of trajectories in time (see also Box E). Most importantly there are not “many worlds” (or exponential many after Everett) but there is only one background free evolutionary landscape populated by a

limited number of macroscopic states (objects, observer) with different fitness (living beings) or stability (objects).

Table 1S. Complexity measures¹:

Kolmogorov complexity:

Bit length of most compact program yielding the same output as process i:

$$K_i = \min [\text{bitlength (compact program for process i)}]$$

Chaitin complexity:

As long as the total bit content of the system counting all stochastic binary decision / switches made in the system;
„stochastic machine code“, average stopping probabilities

$$C_i = \Sigma (\text{all decisions, switches})$$

O(DNA) complexity:

Chaitin complexity times all interactions including interactions between such Interaction complexes (e.g. protein-protein interactions or mutation events)

$$O(\text{DNA}) = \Pi(\Pi_{ij}(C_i))$$

¹Standard complexity definitions followed Kolmogorov (Schmidhuber, 2002) and Chaitin (2006) and were further extended to cover living systems as explained in the results. Different formulas were tested and prototyping / simulations done using Matlab.

Table 2S. Comparing sizes of different state spaces¹

Environments (“worlds”) with 1, 2, 3 up to 10 parameters are compared for the resulting state space and complexity.

Linear Model: State space of 1, 2 ... 10 states for these different 10 environments (“worlds”). Total state space is now Σ State space (n) which here is just $\Sigma n = (n^2 + n) / 2 = 55$.

Exponential model:

State space of $2^1, 2^2 \dots 2^{10} = 1, 2, 4, \dots 1024$ states. for these different 10 environments (“worlds”). Total state space is now Σ State space (n) which here is $\Sigma 2^n = 2^{(n+1)} - 1$. Thus here already the biggest “world” takes the major part of total state space.

Models and examples from physics. We start from examples regarding the anthropocentric principle [see e.g. P.A.M. Dirac , The Cosmological Constants , “Nature” 139 (1937), p. 323; R.H. Dicke, Dirac's Cosmology and Mach's Principle , “Nature” 192 (1961), pp. 440-441; B. Carter , Large Number Coincidences and the Anthropic Cosmological Principle; B. CARR, M. Rees, The Anthropic Principle and the Structure of the Physical World , “Nature” 278 (1979), pp. 605-612; F. DYSON , Disturbing the Universe , Harper & Row, New York - London 1979; J. Barrow , Anthropic Definitions , “Quarterly Journal of the Royal Astronomical Society” 24 (1983), pp. 146-153; J. Barrow, F. Tipler, The Anthropic Cosmological Principle , Clarendon Press, Oxford 1986; J. Demaret, D. Lambert, Le principe anthropique. L'homme est-il le centre de l'Univers? , Armand Colin, Paris 1994].

The examples concern the fine tuning of physical constants [in particular the four natural constants for the intensity of the interaction of the four fundamental forces, respectively α_g (gravitational), α_e (electromagnetic), α_w (electro-weak nuclear), and α_s (strong nuclear)]. However, for the argument here we note ew that for each of the examples that without the feature not only the existence of the observer is not possible (= anthropocentric principle) but *the state space becomes much smaller*: The lack of fine tuning leads often to a collapsed or generally more unstable and *much less complex* worlds (worlds lacking specific sources of complexity, such as worlds without atoms, lacking hydrogen or helium or matter at all, or worlds without stars, water or carbon).

Some Examples (according to INTERS – Interdisciplinary Encyclopedia of Religion and Science, edited by G. Tanzella-Nitti, P. Larrey and A. Strumia, see <http://www.inters.org> for further details on the anthropocentric principle regarding these examples):

- After about 1 sec of time from the beginning of the *Big Bang*, neutrinos decoupled from the rest of the matter, “freezing” the ratio between the number of protons and the neutrons. This depends very sensitively upon the expansion rate i.e. α_g and on the intensity of the weak interaction α_w regarding the decay of the neutron.
- Formation of primordial helium from the *Big Bang* not in the stars depends on the relationship between the total number of protons and neutrons and, thus, upon the value of the ratio α_g/α_w . If this ratio is slightly higher, all protons would be transformed into nuclei of helium, with devastating consequences such as the lack of hydrogen and water. In contrast, an inferior value loses the abundance of cosmological helium, with negative influences for the subsequent thermodynamic evolution of the stars (extremely rapid star evolution, the time of existence of the star becomes in general too short for life to develop on planets.
- α_g determines the initial rate of expansion of the universe: a higher value implies the collapse of the whole universe on itself, more or less immediately, therefore preventing any following “development of the facts”; on the other hand, a value just a little bit lower, would have prevented the subsequent formation of any gravitational aggregation of matter, thereby inhibiting the formation of galaxies and stars and, *a fortiori* , of planets.
- The ratio α_s/α_e is critical for chemistry. Their equilibrium, prevailing the strong nuclear force in the interactions at a very short range, make possible the existence and stability of atomic nuclei, and allow

the formation of a “periodic table” of chemical elements. If α_e had been just a little bit larger, or α_s a little bit smaller, even the lightest nuclei would not have been stable. Similar the exact value of the elementary electrical charge e is important for our chemistry.

- In the formation of proto-stellar masses from interstellar gas it surprisingly happens that the temperature due to contraction reaches the threshold necessary for the nuclear reactions to take place, just before that the same collapse would drive the proto-star towards an irreversible equilibrium of degenerate gas. If such a threshold of temperature was not reached just on time, the universe would be populated by an extremely large number of “failed” stars, but not one energetically active star. Similarly, such ratios guarantee long and stable stars for millions or billions of years (main sequence) before finally contracting into degenerate stars such as white dwarfs.
- Furthermore, we need a significant number of stars in each galaxy to die as a *supernovae* to eject heavy elements into interstellar clouds and later protoplanets. For that new delicate numerical constraints must be imposed to the values of α_g and of α_w . It is in fact required that the many neutrinos produced in the phase immediately preceding the gravitational collapse, which the instability of the star brings about, can interact with the gaseous layers of the star, pushing them violently towards the outer space, an event that occurs only if the rate of interaction and the rate of collapse, that are governed by the two constants above, are constructively compatible with each other.
- *This goes on for every step reaching closer to life*, e.g. the existence of carbon is a delicate nuclear reaction through beryllium and helium ($\text{Be}^8 + \text{He}^4 \rightarrow \text{C}^{12}$), as well as regarding oxygen (e.g. for water), through the capture of new helium nuclei ($\text{C}^{12} + \text{He}^4 \rightarrow \text{O}^{16}$). In the first case, the existence of an opportune energy level of the excited carbon (7,65 Mev) close to the sum of the energy levels of beryllium and helium (7,37 Mev), turns out to strongly favour the carbon synthesis, since the beryllium-helium reaction has a very small cross section. In the second case, if the energy level of the oxygen (7,12 Mev) were not lower than the sum of the energy levels of the two nuclei that produce it (7,16 Mev), almost all the carbon would be completely burnt to produce oxygen, preventing the development of a carbon-based life. Luckily for us, the beryllium, less important for life, is lost, and a good quantity of carbon, without which the whole biology would not be possible, is conserved. The formation of the crystals and the stability of the macromolecules are, moreover, also linked to the critical values of the ratio between the proton and electron masses and of the electrical charge e . Finally, water, so important for life, can be abundantly present at the liquid phase because the average temperature of the biosphere on the surface of the Earth actually falls within the tight interval between its freezing and boiling points (0-100°C). The inventory of the delicate physical and chemical conditions considered “anthropic” is easily further extended (Barrow and Tipler, 1986; Demaret and Lambert, 1994).

In general, the complete state space $S = \sum S_{w_i}$ summarizes over all environments (“worlds”) w . Each w_i has a state space S_{w_i} . Depending on the number p_{ji} of parameters in each of these worlds or environments we have

$$S = \sum (f(m_i) p_{ji}) .$$

Already for moderate non-linear functions $f(m_i)$ (e.g. exponential) the parameter-rich worlds (or, more moderate, the environments which favour stable conditions and complexity) take large slices of the total state space.

¹State space sizes and complexity measures were compared in different definitions and versions using matlab.

Box G. Gödel limit crossing decision in living systems and implications.

We briefly summarize the Gödel proof for decision limits in formal systems as given by Hofstadter, 1979 (see also Felder, 1996). Next we illustrate that cellular systems have the same self referring capabilities (self reference including arithmoquination capabilities) but nevertheless can deal with such system states. Finally biological implications of such a Gödel crossing are discussed.

1. Express with simple symbols all types of logical statements.

Formal systems: Here you can use for instance TNT (Theoria Numerorum Typographica; Hofstadter, 1979, Felder, 1996) a short hand to express mathematical statements using simple symbols. There are standard mathematical symbols such as +(plus), *(times), and =(equals). There are *variables*, represented by the letter a followed by primes: a, a', a'', etc. There are standard logical symbols such as ~ (not), V (or), E (there exists) and A (for all). Finally, there are numbers, which are represented by the two symbols 0 (meaning zero) and S (meaning "the successor of"); so we count 0, S0, SS0, SSS0, and so on.

Starting from a list of axioms such as the Peano axioms

Axiom 1: $\forall a: \sim Sa=0$

Axiom 2: $\forall a:(a+0)=a$

Axiom 3: $\forall a:Aa':(a+Sa')=S(a+a')$

Axiom 4: $\forall a:(a*0)=0$

Axiom 5: $\forall a:Aa':(a*Sa')=((a*a')+a)$

Any type of proof and sentence on natural numbers can be formulated, e.g. $\sim \exists a:a*a=SS0$ would be translated as "There is no square root of two." A sentence or statement is *true* if it can be formed from the axioms. If the statement is *false*, we can derive its converse from the axioms. A Gödel statement G has a truth value which can not be decided from the system though it can be derived from the system.

Cellular systems: Any type of cellular process can be encoded by genes which in turn yield gene products. Operations such as plus and times happen already on the nucleotide level. Variables are in this context genes and gene names, for these exist also the standard logical symbols such as NOT active, OR (one of two gene product), E (there exists a gene such as ...) and A (for all genes applies ...).

2. Formal systems: The **critical step** concerning the Gödel proof is a statement such as: "Sentence G: This statement is not a theorem of TNT."

Cellular systems: Here this would translate into a statement such as: "This cell cycle state is not in the internal stored genetic model."

3. Formal systems: For the Gödel proof a **Gödelization** (give gödel numbers to statements) is necessary to achieve self referring states (Felder, 1996).

Mathematical Logic	TNT	Gödel-numbered TNT
An <u>axiom</u> is an "obvious" statement about natural numbers.	An <u>axiom</u> is a statement string	An <u>axiom</u> is a number
A <u>rule of production</u> is a logical way to work with axioms.	A <u>rule of production</u> is an allowed string-manipulation mechanism.	A <u>rule of production</u> is an allowed mathematical function.
The <u>theorems</u> you produce are new statements about natural numbers.	The <u>theorems</u> you produce are new strings.	The <u>theorems</u> you produce are new numbers.

4. Finally, Writing Sentence G:

a) first incomplete effort

T: The arithmoquine of A is not a valid TNT theorem-number.

A: Sentence T is not a valid TNT theorem-number.

However, this Sentence A is not the sentence G we're looking for, since it isn't about itself, it's about sentence T. We thus put:

T: The arithmoquine of A is not a valid TNT theorem-number.

A: The arithmoquine of Sentence T is not a valid TNT theorem-number.

b) Hence, better and more accurate:

G: The arithmoquine of "The arithmoquine of A is not a valid TNT theorem-number" is not a valid TNT theorem-number.

Cellular systems: In cellular systems the internal stored information starts also from genetic encoded axioms (so certain genes or sets of genes set basic circuits and internal values). A rule of production is a certain type of genetic circuit. And the combination or interference of genetic circuits produces more complex genetic circuits. The last sentence makes clear that the Gödelization and also the arithmoquination happen on the level of genetic circuits, in particular do genetic circuits deal also with the state of the complete cell as a whole and / or can refer to themselves or even to themselves while describing internally the state of the whole cell, too (e.g. in cell cycle, Fig. 3), e.g. a cellular representation of

G: The arithmoquine of "The arithmoquine of A is not a valid TNT theorem-number" is not a valid TNT theorem-number. would be

"The cell cycle state referring to cell cycle control of G₁ to S by activity of cdc25 on cdc2 is blocking the cell cycle control inhibition regarding transition of G₁ to S activated by wee 1 mediated cdc2/cyclin B kinase phosphorylation which is itself controlling activity of cell cycle state."

Interestingly, simulating such cellular conditions (e.g. using Cytoscape, see Fig. 2) referring to the whole cell and involving large genetic circuits shows that often opposing signals can lead "to blocks" of the system (e.g. not only regarding cell cycle but also decisions such as apoptosis vs proliferation). However, as besides the internal information there is also the actual enzymatic activity encoded from the circuit, a clear behaviour arises in most cases in finite time with a clear preference for one state (sometimes including a "blocked" state but then also with biological meaning and selection advantage, e.g. G₀ phase in differentiated cells). Note furthermore, that the system behaviour on the phenotypic side (so beyond the internal representation capabilities of the system) is selected by the environment (itself part of a potential infinite context) for the benefit and best survival capabilities of the organism. Thus "crossing the Gödel limit" happens often in living beings in complex decisions affecting the survival of the whole cell or higher organism and regarding the decision between different survival strategies.

Examples include apoptosis versus proliferation, recombination or none as well as proliferation or differentiation. The identification of the best survival strategy or cell cycle replication (Figure 3) strategy at a given environmental condition is in fact a non decidable Gödel problem for a formal system considering the complexity and stochasticity of the transitions and interactions involved and the potential unlimited environment. The calculation of mutation effects in regulatory proteins for fitness and survival, e.g. mutations in cdk2 is similarly challenging. There are further levels of complexity added in multi-cellular and neural organisms. Detailed calculation and application examples include e.g. the decision of RIP protein between apoptosis or replication where details of the interaction surfaces and the sequence of protein encounters determine the resulting decision (Thakar et al., 2006) or the triggering of a differentiation signal versus malignant proliferation where concentrations and

ratios of two different isoforms of Raf, B-Raf and C-Raf, determine cellular fate (Robubi et al., 2005). Stochastic processes in the cell result from this. In general they describe the complex cellular adaptive behaviour better (e.g. Suel et al., 2006) than non-stochastic models (e.g. for the important cell cycle transition from G_1 to S, reactome map [REACT_1783.2](#)). The same reasoning applies to complex decisions by higher organisms as well as regarding machine-implemented complex decision processes (including nano-machines).