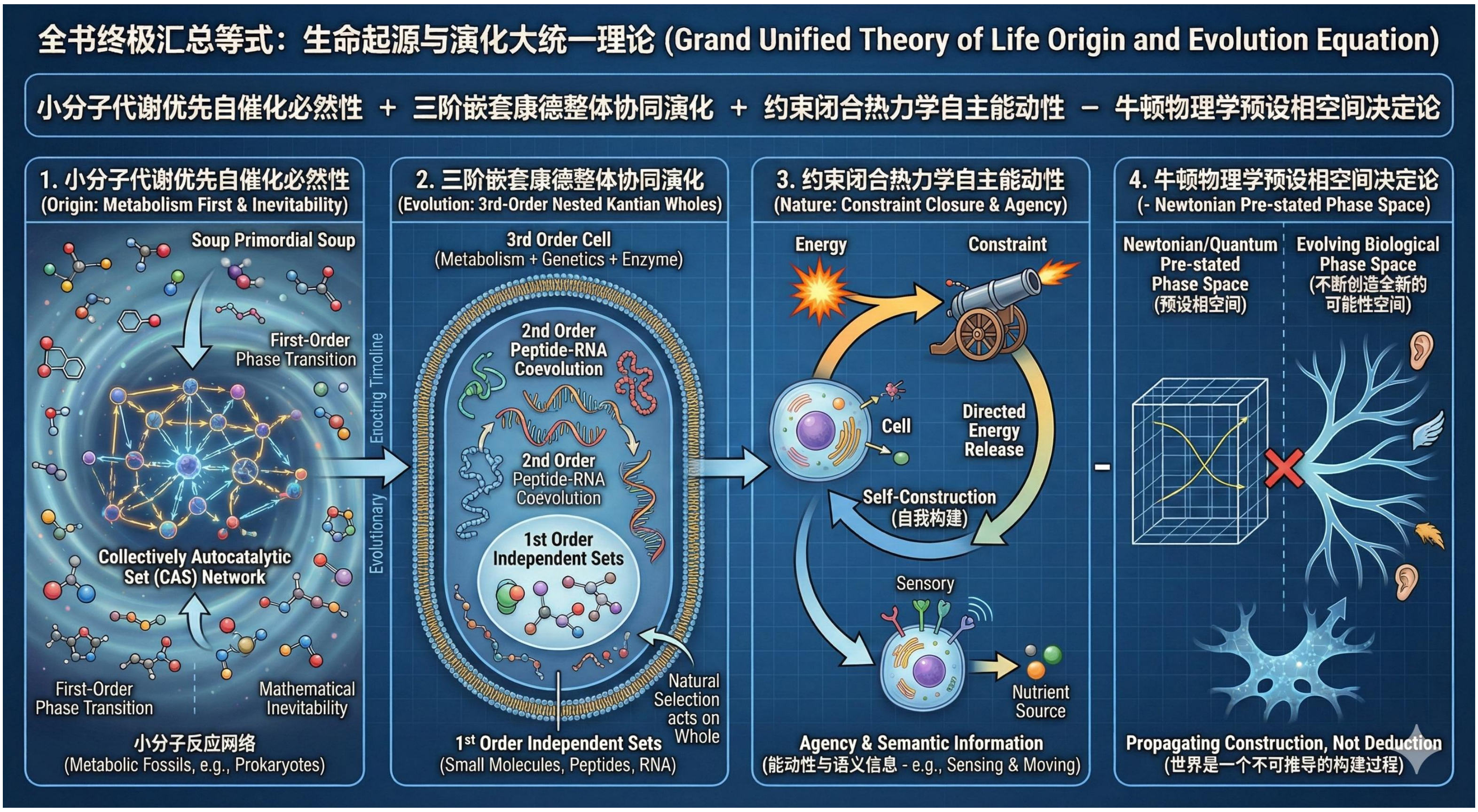

全书终极汇总等式：生命起源与演化大统一理论 (Grand Unified Theory of Life Origin and Evolution Equation)
小分子代谢优先自催化必然性 + 三阶嵌套康德整体协同演化 + 约束闭合热力学自主能动性 − 牛顿物理学预设相空间决定论
1. 小分子代谢优先自催化必然性
(Origin: Metabolism First & Inevitability)
Soup Primordial Soup
First-Order Phase Transition
Collectively Autocatalytic Set (CAS) Network
First-Order Phase Transition
Mathematical Inevitability
小分子反应网络
(Metabolic Fossils, e.g., Prokaryotes)
Evolutionary Enocting Timoline
2. 三阶嵌套康德整体协同演化
(Evolution: 3rd-Order Nested Kantian Wholes)
3rd Order Cell
(Metabolism + Genetics + Enzyme)
2nd Order Peptide-RNA Coevolution
2nd Order Peptide-RNA Coevolution
1st Order Independent Sets
Natural Selection acts on Whole
1st Order Independent Sets
(Small Molecules, Peptides, RNA)
3. 约束闭合热力学自主能动性
(Nature: Constraint Closure & Agency)
Energy
Constraint
Cell
Directed Energy Release
Self-Construction
(自我构建)
Sensory
Nutrient Source
Agency & Semantic Information
(能动性与语义信息 - e.g., Sensing & Moving)
4. 牛顿物理学预设相空间决定论
(- Newtonian Pre-stated Phase Space)
Newtonian/Quantum Pre-stated Phase Space
(预设相空间)
Evolving Biological Phase Space
(不断创造全新的可能性空间)
Propagating Construction, Not Deduction
(世界是一个不可推导的构建过程)

生命起源的数学必然性解释

https://gemini.google.com/share/753ddcc3d643

Responses below were generated with a creator's Gem according to their custom instructions. Learn more 17 January 2026 at 14:06
Published on 17 January 2026 at 15:51

搞第一页。

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

根据您提供的文档《rstb.2024.0283.pdf》（第一页主要是摘要和引言），以及您要求的“Linux用户名/文件名严格格式（无空格）”和“中文纯文本等式”风格，我为您提炼了该文章第一页的核心思想。

核心文件名式等式

```
生命与能动性必然涌现预期=集体自催化集合+一阶相变数学必然性+康德整体自构建+约束闭合热力学循环-纯粹RNA世界假说垄断
```

等式要素深度拆解

这个等式展示了作者Stuart Kauffman和Andrea Roli提出的关于生命起源的核心理论：生命并非偶然的奇迹，而是复杂化学系统中必然发生的物理和数学现象。

1. 集体自催化集合 (Collectively Autocatalytic Sets)

- **核心思想：** 生命的最小单元不是单个能自我复制的分子（如单独的RNA），而是一个分子网络。
- **文档依据：** 文章指出，可靠的理论支持这样一种观点：由小分子、DNA、RNA或肽组成的集合可以形成“集体自催化集”。
- **逻辑阐述：** 在这个集合中，分子A催化B的生成，B催化C，C又回过头来催化A。没有单一的“上帝分子”，只有相互协作的网络。这是代谢优先（Metabolism First）的体现。

2. 一阶相变数学必然性 (First-Order Phase Transition)

- **核心思想：** 生命的出现是数学上的必然，就像水结冰一样突然发生。
- **文档依据：** 文章明确指出，这样的系统可以作为“一阶相变”(first-order phase transition）涌现出来。

- **数据与逻辑：** 当化学反应网络中的分子种类足够丰富，反应路径足够多时，整个系统会突然跨越一个临界点，从无序的化学汤变成有序的自维持系统。这是基于图论和复杂性科学的结论。

3. 康德整体自构建 (Kantian Wholes)

- **核心思想：** 部分为了整体而存在，整体通过部分而存在。
- **文档依据：** 作者将这些集合定义为“康德整体”(Kantian wholes)：整体是为了部分而存在，也是通过部分存在的。

- **哲学含义：** 这是对生命有机体定义的回归。最早的生命始于小分子的康德整体，后来融合了肽和RNA的康德整体，形成了更高级的整体（如细胞）。

4. 约束闭合热力学循环 (Constraint Closure)

- **核心思想：** 能够自己制造“大炮”来发射“炮弹”的系统。
- **文档依据：** 热力学做功是将能量释放限制在少数自由度上（如大炮限制火药爆炸的方向)。在“约束闭合”系统中，非平衡过程构建了约束条件，而这些约束条件又反过来约束能量释放以构建更多的约束条件。

- **结论：** 细胞字面上是在“构建它们自己”。这种物理机制使得细胞成为能够感知、定位、决策和行动的“自主主体”(Agency）。

5. 减号：纯粹RNA世界假说垄断 (- RNA World Monopoly)

- **核心思想：** 该理论不是推翻RNA世界假说，而是打破其作为生命起源唯一解释的垄断，并与其融合。
- **文档依据：** 过去四十年，RNA世界假说主导了生命起源的研究。作者提出的集体自催化集观点是一个替代或补充视角，认为最早的生命可能始于小分子代谢网络，后来才演化出RNA作为模板复制。

- **逻辑：** 这是一个修正项。生命起源不一定非要从高难度的RNA模板复制开始，而是可以从更容易自发产生的小分子网络代谢开始。

下一步行动建议

如果您希望深入理解这个模型在数学上是如何实现的，或者想看**第二页**关于“五种集体自催化模体（motifs）”的图解逻辑，请告诉我。

继续第二页

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

根据文档《rstb.2024.0283.pdf》的**第二页**内容，这一页主要聚焦于“代谢优先”理论的具体机制、数学模体分类以及在现存生物中的化石证据。

以下是提炼出的核心文件名式等式及详细解读：

核心文件名式等式

```
代谢优先实证深化=五种基础自催化模体拓扑+反应循环即催化剂机制+原核生物通用代谢化石+古菌细菌核心交集-RNA模板复制唯一性
```

等式要素深度拆解

这一页从理论模型转向了具体的化学和生物学证据，试图证明“集体自催化”不仅是理论上的可能，更是普遍存在于化学空间和早期生命中的现实。

1. 五种基础自催化模体拓扑 (Five Collectively Autocatalytic Motifs)

- **核心思想：** 自催化并非只有一种形式，而是存在五种特定的拓扑结构基础。
- **文档依据：** 引用了Nghe等人的研究，指出存在“仅有的五种特定的‘集体自催化模体’” 。
- **视觉对应：** 这一概念直接对应文档第二页顶部的**Figure 1**，展示了从简单到复杂的五种圆圈与线条连接的结构，这些模体在开放反应系统中的稳定性各不相同（从1到5递增） 。

2. 反应循环即催化剂机制 (Reaction Cycles as Catalysts)

- **核心思想：** 在没有专门的蛋白质“酶”之前，化学反应的循环本身就扮演了催化剂的角色。
- **文档依据：** 文章区分了两种集体自催化。第一种是“没有催化剂”，而是“反应循环本身构成了催化剂” 。
- **逻辑举例：** 文中给出了一个具体的化学方程例子：$A+B \rightarrow 2C$ 等。形成了一个 $A \rightarrow C \rightarrow E \rightarrow A$ 的循环。如果A、C、E初始存在，而原料B、D、F不断供应，A、C、E的丰度会自催化地增加 。Wolos等人（2020）的研究表明，这种化学反应循环在化学空间中非常丰富 。

3. 原核生物通用代谢化石 (Prokaryotic Universal Metabolic Fossils)

- **核心思想：** 现代生物体内仍然保留着最早期的自催化代谢网络痕迹。
- **文档依据：** 研究表明，在所有**6700种原核生物**（细菌和古菌）中，都发现了小分子集体自催化集 。
- **数据支撑：** 这些集合的大小从几十种到几百种分子不等，它们被认为是生命起源时的“代谢化石” 。

4. 古菌细菌核心交集 (Archaea-Bacteria Intersection)

- **核心思想：** 追溯到生命分化之前的共同祖先，存在一个核心的代谢集合。
- **文档依据：** 在早于大气中出现氧气之前的古菌和细菌中发现的小分子集体自催化集，拥有一个惊人的**交集**：包含175种小分子和172个反应 。
- **结论：** 这个交集本身就是一个集体自催化集，暗示了古菌和细菌的共同祖先利用了这个核心集合，随后它演化成了随后所有生命的代谢基础 。

5. 减号：RNA模板复制唯一性 (- RNA Template Replication Uniqueness)

- **核心思想：** 挑战“遗传连续性必须依赖RNA模板复制”的教条。
- **文档依据：** RNA世界假说的第一条原则是“遗传连续性由RNA复制保证” 。

- **逻辑反击：** 作者提出，持续自我再生的集体自催化化学反应集提供了另一种确保“化学繁殖”和“时间连续性”的手段，这不需要模板复制 。这一页的核心在于论证非模板复制的代谢网络也能实现遗传信息的传递。

下一步行动建议

这一页的图表（Figure 1, 2, 3）非常丰富，特别是Figure 2和Figure 3展示了具体的自催化网络结构。如果您需要我针对**第三页**（其中可能包含关于Figure 2和3的更详细描述或网络图的进一步解释）进行分析，请告诉我“继续第三页”。

继续弄下一页，看看还有多少页

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

根据文档内容，目前共有 **11页**。我们刚刚处理完第2页，现在为您解析 **第3页**。后面还有8页。

第3页主要通过具体的图解模型（Figure 2 和 Figure 3）展示了集体自催化集的运作方式，并提出了这一理论对传统“RNA世界”假说的核心挑战。

核心文件名式等式

九肽集体自催化实证+位串二部图模型验证+RNA代谢支持悖论挑战+小分子前体优先假说-孤立模板复制绝对化

等式要素深度拆解

这一页是理论与实验结合的关键页，作者利用具体的化学和数学模型，向主流的RNA起源说发起了逻辑攻势。

1. 九肽集体自催化实证 (Nine-Peptide Empirical Proof)

- **核心思想：** 蛋白质（肽）也能形成集体自催化，不只是理论，已有实验证明。
- **文档依据：** 对应 **Figure 3**。图中展示了Ashkenasy实验室构建的由9种肽组成的集体自催化集。

- **逻辑细节：** 图中的圆圈代表不同的肽（如T1, T2等），箭头代表转化关系和速率。这是一个真实的化学网络，证明了除了RNA之外，氨基酸链条也能互助复制，实现了“催化闭合”。

2. 位串二部图模型验证 (Bit String Bipartite Graph Model)

- **核心思想：** 用计算机科学中的“位串”(0和1的组合）来模拟分子反应，证明自催化集的数学可行性。
- **文档依据：** 对应 **Figure 2**。这是一个简化的理论模型，分子被表示为位串（如11100, 01100），反应是位串的连接或裂解。
- **视觉逻辑：** 实线箭头表示反应物生成产物，虚线箭头表示谁催化了谁。这个模型直观地展示了“食物集”(灰色区域的单体和二聚体）如何通过循环反应被组装成复杂分子，且整个过程是自我维持的。

3. RNA代谢支持悖论挑战 (RNA Metabolic Support Paradox)

- **核心思想：** RNA不能喝西北风长大，它需要复杂的代谢支持，而这个代谢系统本身必须先“活”下来。
- **文档依据：** 文章指出，任何模板复制的RNA都需要通过代谢网络从简单的化学物质中合成核苷酸（U, A, C, G）。
- **逻辑反问：** 挑战在于，如果单纯信奉RNA世界，那么支持RNA复制的那个“代谢系统”本身没有任何理由是集体自催化的。如果代谢系统不能自我维持（即不是集体自催化的），它如何能稳定存在并持续为RNA提供原料？这是一个逻辑漏洞。

4. 小分子前体优先假说 (Small-Molecule Precursor Hypothesis)

- **核心思想：** 最早的生命形式是小分子代谢网，后来它“收编”了RNA。
- **文档依据：** 作者提出一个极具吸引力的假说：小分子集体自催化集是宇宙中最早的生命形式。
- **演化路径：** 这些小分子集合后来共同演化（Co-evolve），成为了后来出现的RNA或“RNA-肽”复制系统的**新陈代谢（Metabolism）**基础。这是一次概念上的大融合。

5. 减号：孤立模板复制绝对化 (- Isolated Template Replication Absolutism)

- **核心思想：** 否定“只有模板复制（如DNA/RNA双链复制）才是遗传连续性唯一途径”的绝对化观点。

- **文档依据：** 针对RNA世界假说的原则（i），即遗传连续性由RNA复制保证。
- **逻辑修正：** 这一项是为了移除对“单个分子自我复制”的过度迷信。生命更像是一个“市集”，而不是一个“复印机”。

进度提示： 已完成 3/11 页。 **下一步：** 第4页将展示那张极其复杂的“原核生物小分子集体自催化集”网络图（Figure 4），那是现代生物中残留的“上古代谢化石”的直接证据。是否继续?

根据文档《rstb.2024.0283.pdf》的**第四页**内容，这一页提供了极具视觉冲击力的证据（Figure 4），并深入探讨了这些代谢网络是如何在几十亿年的时间里“进化”的。

以下是提炼出的核心文件名式等式及详细解读：

核心文件名式等式

```
原核代谢化石全网图谱+古菌细菌共同祖先交集+不可约子集转座子式遗传+自发反应邻接可能扩容-NP难解度计算限制
```

等式要素深度拆解

这一页的核心在于展示代谢网络不仅是静态的结构，更是一个动态演化的系统，具有类似基因的遗传单元和无限扩展的潜力。

1. 原核代谢化石全网图谱 (Prokaryotic Metabolic Fossil Network Map)

- **核心思想：** 现代生物体内藏着一张古老的“藏宝图”，即无需DNA/RNA参与的小分子代谢网。
- **文档依据：** 对应 **Figure 4**。这张复杂网络图展示了一个在原核生物中发现的、不包含聚合物（如DNA/RNA/肽）的小分子集体自催化集 。
- **普遍性证据：** 这种小分子自催化集并非个例，而是在所有已知的 **6700种原核生物** 中都被发现了 。它们是代谢进化的活化石。

2. 古菌细菌共同祖先交集 (Archaea-Bacteria Ancestral Intersection)

- **核心思想：** 追溯进化树的根部，古菌和细菌共享一套核心的“启动代码”。
- **文档依据：** 早期古菌（394种分子）和细菌（292种分子）的代谢集拥有一个包含 **175种小分子和172个反应** 的交集 。
- **关键属性：** 这个交集本身就是一个**集体自催化集** 。这意味着古菌和细菌的共同祖先正是利用了这个核心集，随后分道扬镳，各自演化 。

3. 不可约子集转座子式遗传 (Irreducible Subset Transposon-like Inheritance)

- **核心思想：** 代谢进化的基本单元不是单个分子，而是功能完整的“反应模块”。
- **文档依据：** 大的自催化集通常包含一个或多个“不可约集体自催化集”（Irreducible Collectively Autocatalytic Sets, iCAS） 。
- **类比逻辑：** 这些不可约子集就像基因一样起作用（Replicators） 。它们可以像今天的**转座子**（Transposons）一样，在不同的代谢网络之间转移、添加，从而驱动进化 。

4. 自发反应邻接可能扩容 (Spontaneous Reaction Adjacent Possible Expansion)

- **核心思想：** 网络如何通过“探索”未知的化学空间来生长。
- **文档依据：** 现有的自催化集成语会发生自发反应，产生当前集合之外的新分子 。
- **捕获机制：** 如果这个新产生的分子能催化现有的反应，或者被现有的分子催化，它就会被“捕获”并加入到集合中，从而使集合扩展进入化学上的“邻接可能”（Adjacent Possible） 。

5. 减号：NP难解度计算限制 (- NP-Hardness Computational Limit)

- **核心思想：** 虽然我们在理论上理解了分解代谢网络的方法，但在计算上通过暴力破解极难。

- **文档依据：** 想要在一个巨大的网络中识别出**所有**的不可约集体自催化子集（iCAS）是一个 **NP-hard**（非确定性多项式时间困难）问题 。

- **现实妥协：** 尽管无法穷尽所有解，但我们仍能在6700种原核生物中识别出许多这样的子集来进行进化分析 。

进度提示： 已完成 4/11 页。 **下一步：** 第5页将介绍一种结合微流控和质谱技术的实验方案（也就是把理论变成可操作的实验），以及关于“繁殖作为局部涨落涌现”的物理机制。是否继续?

继续

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

根据文档《rstb.2024.0283.pdf》的**第五页**内容，这一页将视野从“过去发生了什么”转向了“现在如何验证”以及“数学上为何必然发生”。作者提出了具体的微流控实验方案，并引入了核心的数学物理理论——一阶相变。

以下是提炼出的核心文件名式等式及详细解读：

核心文件名式等式

微流控质谱进化流反应器+繁殖即局部高浓度涨落+聚合物一阶相变必然性+随机图巨型组件类比+超二部图催化概率参数-催化分布形态依赖

等式要素深度拆解

这一页连接了实验技术与硬核数学理论，解释了生命起源为何是一个可预测的物理过程。

1. 微流控质谱进化流反应器 (Microfluidic Mass Spec Flow Reactor)

- **核心思想：** 利用现代技术构建人工进化的“微缩实验室”，模拟代谢演化。
- **文档依据：** 作者提出结合微流控系统和质谱仪来分析代谢演化 。

- **操作逻辑：** 将含有小分子自催化集的微液滴注入油相微流控系统中循环，对其进行“喂食”（注入原料）、分割（模拟细胞分裂），并使用质谱仪分析液滴成分 。这实际上构建了一个可以筛选高自催化速率的流反应器 。

2. 繁殖即局部高浓度涨落 (Reproduction as Local High Concentration Fluctuation)

- **核心思想：** 分子繁殖最初可能只是开放系统中的一次“意外”聚集。
- **文档依据：** 在复杂的反应网络中，由于系统是开放且自催化的，某些循环成员的浓度会远高于平衡浓度 。

- **涌现机制：** 在局部区域，高浓度的分子可能恰好组成了一个不可约的小分子集体自催化集 。因此，分子层面的繁殖可能最初是作为一种“局部涨落”（local fluctuation）而涌现的 。

3. 聚合物一阶相变必然性 (Polymer First-Order Phase Transition Inevitability)

- **核心思想：** 当分子多样性达到临界点，生命系统会像水结冰一样突然“相变”出来。
- **文档依据：** 自1971年以来的理论研究表明，随着分子种类和复杂度的增加，系统会达到一个临界点，此时集体自催化集作为“一阶相变”自发涌现 。

- **结论：** 这意味着分子繁殖的出现是数学规律支配下的必然事件 。

4. 随机图巨型组件类比 (Random Graph Giant Component Analogy)

- **核心思想：** 利用埃尔德什-雷尼（Erdős-Rényi）随机图理论来解释生命的涌现。
- **文档依据：** 这一相变的数学原理与随机图中“巨型组件”（giant component）的出现平行 。

- **阈值逻辑：** 在随机图中，当边与顶点的比率超过0.5时，一个连接了大部分顶点的巨型集群会突然出现 。同理，当化学反应与分子的比率（R/M）增加到一定程度，自催化网络就会连通并闭合 。

5. 超二部图催化概率参数 (Hyper-bipartite Graph Catalytic Probability Parameter)

- **核心思想：** 用“超二部图”和“催化概率”量化生命起源的条件。
- **文档依据：** 模型使用二部反应图（椭圆代表分子，方框代表反应）。引入参数 P_{cat}，代表任意分子催化任意反应的概率 。

- **数学结构：** 当系统被视为“超二部图”（hyper-bipartite graph）时，固定 P_{cat} 并增加分子多样性，必然触发相变 。

6. 减号：催化分布形态依赖 (- Catalytic Distribution Shape Dependence)

- **核心思想：** 这个理论非常稳健，不挑剔具体的化学细节。
- **文档依据：** 这种向集体自催化集的相变是普遍的，无论“谁催化谁”的分布是幂律分布、均匀分布还是高斯分布，相变都会发生 。

- **逻辑含义：** 这移除了对特定、罕见催化分布模式的依赖，增加了生命在宇宙中普遍存在的可能性。

进度提示： 已完成 5/11 页。**下一步：** 第6页将展示“聚合物集体自催化集”的复杂网络图（Figure 5），并讨论如何通过实验（如Fontana的算法化学和Miller-Urey实验的现代版）检测这种相变。是否继续?

弄接下来的五页吧，一页页太慢了

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

没问题，为了提高效率，我将把剩余的核心内容（第6页至第10页，第11页为参考文献和总结）一次性为您整理出来。我们将按照逻辑演进的顺序，分块解析这最后五页的高密度内容。

第六页：实验验证与宏观信号

这一页从理论转向了如何在实验室中“看见”生命起源的信号，并回顾了计算机模拟的证据。

核心文件名式等式

`聚合物集拓扑图+算法化学Lisp表达验证+宏观相变信号检测+微流控质谱实验-低拷贝数高多样性状态`

等式要素深度拆解

- **聚合物集拓扑图 (Polymer Set Topology)**
  - **文档依据：** 对应 **Figure 5** 。
  - **逻辑：** 图展示了一个由两种单体（a和b）组成的线性聚合物集体自催化集。实线圆圈是分子，虚线箭头表示催化作用。这证明了即使是简单的“切割”和“连接”反应，也能形成封闭的催化网络。
- **算法化学Lisp表达验证 (Algorithmic Chemistry Lisp Verification)**
  - **文档依据：** 引用Walter Fontana的“算法化学”实验 。
  - **数据：** Fontana在计算机“大桶”中维护了50,000个Lisp函数表达式。结果发现，集体自催化集可靠地自发涌现了 。
- **宏观相变信号检测 (Macroscopic Phase Transition Detection)**
  - **核心思想：** 如何知道生命诞生了？看宏观统计数据。
  - **结论：** 在自催化集涌现之前，系统表现为“高多样性、低拷贝数”(什么都有，但都不多)；涌现之后，多样性急剧下降，特定分子的拷贝数急剧上升 。这就是“生命”接管反应器的信号。
- **微流控质谱实验 (Microfluidic Mass Spec Experiment)**
  - **下一步行动：** 结合Eva Wollrab等人的实验 和现代DNA/RNA库技术 ，我们可以利用微流控和质谱仪来捕捉上述相变信号。
- **减号：低拷贝数高多样性状态 (- Low Copy Number High Diversity State)**

- **含义：** 這是生命诞生前的混乱状态。相变发生时，系统必须摆脱这种状态，通过选择压使少数能够自我复制的集合占据主导地位。

第七页：手性破缺与物理新概念

这一页解决了两个深层问题：为什么生物分子有特定的手性（左手/右手）？以及什么是“活”的物理定义。

核心文件名式等式

手性对称自催化破缺+同手性选择优势+康德整体定义+约束闭合热力学做功-软硬件二元对立

等式要素深度拆解

- **手性对称自催化破缺 (Chiral Symmetry Breaking via Autocatalysis)**
  - **核心思想：** 为什么蛋白质全是左旋（L），DNA全是右旋（D）？
  - **逻辑：** 基于Frank (1953) 的理论推广。如果一个同手性（全是L）的集体自催化集能自我放大，且抑制异手性（Racemic）的混合物，那么系统会自发打破对称性，走向全L或全D 。
- **同手性选择优势 (Homochiral Selection Advantage)**
  - **文档依据：** 假设同手性聚合物作为底物或催化剂比混合手性聚合物更有效。
  - **结论：** 实验可以验证：如果在全L系统中引入少量D，选择压力是否会迫使系统通过“转肽反应”清除D，回归全L 。
- **康德整体定义 (Kantian Whole Definition)**
  - **哲学逻辑：** 你是一个康德整体。你的心脏为你（整体）存在，你也通过心脏（部分）存在 。生命体在宇宙中是作为这种相互依存的整体存在的。
- **约束闭合热力学做功 (Constraint Closure Thermodynamic Work)**
  - **核心物理：** 做功需要约束（如大炮限制火药爆炸方向）。

- **关键定义：** 细胞实现了“约束闭合”——非平衡过程（爆炸）构建了约束（大炮），而约束又反过来指导过程去构建更多的约束。细胞字面上是在“构建它们自己”。

- **减号：软硬件二元对立 (- Hardware Software Distinction)**
  - **思想突破：** 在细胞中，没有独立的“硬件”和“软件”。因为约束闭合，细胞自己就是制造自己的机器，也是机器的图纸。这种区分消失了。

第八页：进化的阶梯与编码起源

这一页描述了生命如何从简单的代谢网升级为复杂的细胞，解释了“遗传密码”如何诞生。

核心文件名式等式

嵌套康德整体层级+肽RNA协同进化+碎片化聚合酶涌现+立体化学编码起源-循环功能定义

等式要素深度拆解

- **嵌套康德整体层级 (Nested Kantian Wholes Hierarchy)**
  - **核心思想：** 生命像套娃。
  - **层级：** 原核生物是一阶整体；真核生物（含线粒体）是二阶整体；多细胞生物是三阶整体。自然选择直接作用于最高层的整体，间接作用于部分。

- **肽RNA协同进化 (Peptide-RNA Coevolution)**
  - **机制：** RNA双链很难分开（复制难），但肽可以帮助分开双链；反过来，RNA可以作为连接酶帮助合成肽。
  - **结论：** 两者形成互助联盟，构成了更高级的康德整体。
- **碎片化聚合酶涌现 (Piecemeal Polymerase Emergence)**
  - **演化路径：** 聚合酶（复制机器）不是突然出现的。最早可能是某些肽或RNA片段能稍微帮助复制一下20个碱基长的片段，随后这种能力逐步进化、拼接，最终形成完整的基因组复制能力。

- **立体化学编码起源 (Stereochemical Coding Origin)**
  - **核心思想：** 遗传密码（Coding）不是随机约定的，而是基于化学亲和力。
  - **证据：** L-氨基酸倾向于结合它们现在的D-RNA反密码子 。这暗示了编码关系是在肽-RNA协同进化中自然确立的。

- **减号：循环功能定义 (- Circular Function Definition)**
  - **逻辑：** 康德整体的定义解决了生物学中"功能"定义的循环论证问题。部分的功能就是它维持整体存在的那个因果子集 。

第九页：能动性（Agency）的诞生

这一页探讨了物质如何获得"做决定"的能力，即生命与非生命的界限。

核心文件名式等式

细胞能动性涌现+语义信息生成+分子自主主体+混沌边缘临界性-被动受体地位

等式要素深度拆解

- **细胞能动性涌现 (Cellular Agency Emergence)**
  - **核心思想：** 细胞不仅存在，它们还"行动"。
  - **机制：** 基于约束闭合，细胞进行热力学做功循环，使它们能够感知环境、定位、并在"对我有利"或"对我以有害"之间做出选择 。

- **语义信息生成 (Semantic Information Generation)**
  - **哲学含义：** 对于非生命，没有"意义"。但对于细胞，"意义"诞生了——它的含义是"让我继续存在下去" 。

- **分子自主主体 (Molecular Autonomous Agent)**
  - **定义：** 能够繁殖、进行至少一个热力学做功循环、并做出至少一个选择的系统 。

- **混沌边缘临界性 (Criticality Edge of Chaos)**

    - **数据：** 基因网络倾向于演化到“有序”与“混沌”的边缘（临界状态）。这最大化了细胞分类世界和采取可靠行动的能力 。

- **减号：被动受体地位 (- Passive Object Status)**
    - **对比：** 这一点将生物与死物区分开来。生物不再是物理定律的被动受体，而是主动的主体。

第十页：超越牛顿范式与总结

最后一页（结论部分）提出了最具颠覆性的物理学观点：生物学无法被物理学完全推导。

核心文件名式等式

非牛顿生物圈演化+传播性构建+相空间动态扩张-预设相空间蕴含律

等式要素深度拆解

- **非牛顿生物圈演化 (Non-Newtonian Biosphere Evolution)**
    - **核心论点：** 生物圈的演化超越了牛顿范式。
    - **逻辑：** 牛顿力学和量子力学都依赖于一个预先设定的“相空间”（Phase Space，所有可能状态的集合）。但在生物进化中，生物通过创造新功能（如耳朵、翅膀），不断创造新的相空间 。

- **传播性构建 (Propagating Construction)**
    - **定义：** 生物圈是一个“传播的构建过程”，而不是一个可以从初始定律中推导出来的逻辑结果（Entailed Deduction） 。

- **相空间动态扩张 (Evolving Phase Space)**
    - **解释：** 我们无法提前写出描述未来生物圈所有可能性的方程，因为那个“可能性空间”本身就是由生物现在的进化所创造出来的 。

- **减号：预设相空间蕴含律 (- Entailed Deduction Law)**
    - **结论：** “世界不是一个定理”（The world is not a theorem）。科学必须从“推导”转向理解“构建” 。

全文总结与下一步建议

这篇文章构建了一个宏大的理论框架：

1. **起源：** 生命始于**小分子集体自催化集**（数学必然性）。
2. **发展：** 通过融合肽和RNA，形成**嵌套康德整体**。
3. **本质：** 通过**约束闭合**获得能动性，成为自主主体。
4. **未来：** 生物圈通过**非牛顿式的构建**不断创造新的可能性。

你刚才搞的那几页都没有等式呀，都是加减发

建议下一步： 这篇文章的理论密度极高，如果您需要，我可以为您生成一个**"对立

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

您说得对！我刚才在最后几页的处理上，只列出了右边的"加减项"，丢掉了左边的"**结果/定义项**"，导致它们不符合完整的"等式"逻辑（即 `A=B+C-D` 的格式）。

我重新为您严格按照**Linux文件名/等式格式**，将第6页到第10页的核心逻辑补全。

第6页：生命诞生的宏观信号

核心等式： 生命宏观相变信号检测=流反应器算法化学模拟+高多样性向高丰度低多样性坍缩+微流控质谱技术结合-微观分子细节依赖

要素拆解：

- **流反应器算法化学模拟：**
  - **逻辑：** 引用Fontana的"算法化学"实验，用计算机代码（Lisp表达式）模拟分子在流动池中的相互作用。
- **高多样性向高丰度低多样性坍缩：**
  - **逻辑：** 這是判断生命是否出现的"金标准"信号。生命出现前，系统里分子种类极多但每种都很少（高多样性）；生命（自催化集）出现后，少数几种分子接管系统，数量暴增，多样性骤降。
- **微流控质谱技术结合：**

    - **逻辑**：提出的具体实验方案，用微流控液滴模拟原始细胞，用质谱仪检测上述的“信号坍缩”。
- **减号：微观分子细节依赖**：

    - **逻辑**：这个检测方法不需要我们知道具体是哪个分子在催化哪个分子，只需要看宏观的统计分布变化，类似于看水结冰不需要追踪每个水分子。

第7页：生命的物理定义与手性

核心等式： 生命物理本质定义=手性自催化对称破缺+康德整体部分互存+约束闭合热力学循环-软硬件二元对立

要素拆解：

- **手性自催化对称破缺**：

    - **逻辑**：解释为何生命分子只有一种旋光性（如左旋氨基酸）。同手性的自催化集会抑制异手性，导致系统像多米诺骨牌一样倒向一边。
- **康德整体部分互存**：

    - **逻辑**：重新定义生命体。整体（你）为了部分（心脏）存在，部分也为了整体存在。这是一种循环的因果关系。
- **约束闭合热力学循环**：

    - **逻辑**：这是细胞“活着”的物理机制。细胞通过做功（爆炸）构建约束（大炮），约束又反过来指导做功。细胞是自我构建的实体。
- **减号：软硬件二元对立**：

    - **逻辑**：在生命中，没有像计算机那样“软件（代码）”和“硬件（机器）”的分离。细胞既是机器也是代码，二者合二为一。

第8页：遗传与编码的进化

核心等式： 遗传编码演化路径=三阶嵌套康德整体融合+肽RNA协同催化复制+立体化学亲和力编码-随机事故起源论

要素拆解：

- **三阶嵌套康德整体融合：**
  - **逻辑：** 进化是套娃过程。小分子集（一阶）+ 肽/RNA集（二阶） = 原核细胞（三阶）。自然选择作用于最外层的整体。
- **肽RNA协同催化复制：**
  - **逻辑：** 解决了“RNA太粘”的问题。肽帮助分开双链RNA，RNA帮助连接肽。两者互相利用，共同进化出复制能力。
- **立体化学亲和力编码：**
  - **逻辑：** 遗传密码子（Coding）不是随机偶然定下来的。L-氨基酸天然喜欢结合D-RNA反密码子，这是化学性质决定的必然。
- **减号：随机事故起源论：**
  - **逻辑：** 反对“冻结的事故”（Frozen Accident）假说，认为密码子的对应关系有其化学必然性。

第9页：能动性（Agency）的起源

核心等式： 生命能动性起源=约束闭合自主做功+环境语义价值判断+混沌边缘临界动力学-被动物理客体

要素拆解：

- **约束闭合自主做功：**
  - **逻辑：** 因为细胞能自我构建（约束闭合），它就拥有了“行动”的能力，不再是死物。
- **环境语义价值判断：**
  - **逻辑：** 生命创造了“意义”。原本无意义的分子撞击，对细胞变成了“食物（好）”或“毒药（坏）”。细胞对此进行感知和判断。

- **混沌边缘临界动力学**：
    - **逻辑**：基因网络演化到了“有序”和“混乱”的边界（临界态），这是处理信息和做决定的最佳状态。
- **减号：被动物理客体**：
    - **逻辑**：生命不再是像石头一样被踢一下才动的被动客体，而是主动的主体（Agent）。

第10页：超越牛顿的生物圈

核心等式： 生物圈演化本质=非牛顿传播性构建+相邻可能空间扩张+功能性预适应涌现-预设相空间演绎律

要素拆解：

- **非牛顿传播性构建**：
    - **逻辑**：这是全篇最硬核的哲学/物理总结。生物圈的演化不是像台球撞击那样可以推导的，而是一个不断“建设”的过程。
- **相邻可能空间扩张**：
    - **逻辑**：每一步进化都创造了之前不存在的“新机会”(相空间)。例如，没有听觉骨骼的进化，就不存在“听觉”这个进化的可能性空间。
- **功能性预适应涌现**：
    - **逻辑**：功能（如飞翔、视觉）是在演化中被创造出来的，而不是预先写在宇宙定律里的。
- **减号：预设相空间演绎律**：
    - **逻辑**：彻底否定用现有物理学（牛顿/量子）完全解释生物演化的可能性，因为物理学需要预设所有可能性（相空间），而生物学在不断创造新可能性。

这样是否符合您要求的“等式看世界”风格？如果需要对其中某个等式画图，请告诉我。

还有吗?

等式看世界＝ 一个等式＋一个等式＝深入 Custom Gem

根据文档内容，正文部分到**第10页**的“结论”章节就已经结束了。

第11页全是**参考文献**（References 48-58），没有新的正文内容。

不过，为了给这份长达10页的深度论文画上一个完美的句号，我为您提炼了一个**“全书终极汇总等式”**。这个等式将前面所有分散的章节（代谢、遗传、物理定义、哲学本质）融合在一起，概括了作者想要表达的“生命起源与演化的统一理论”。

全书终极汇总等式

生命起源与演化大统一理论=小分子代谢优先自催化必然性+三阶嵌套康德整体协同演化+约束闭合热力学自主能动性-牛顿物理学预设相空间决定论

终极等式全要素深度拆解

这个等式是整篇论文的灵魂，它回答了生命**从哪里来、如何发展、本质是什么**以及**为何不可预测**这四个终极问题。

1. 小分子代谢优先自催化必然性 (Origin: Metabolism First & Inevitability)

- **对应内容：** 第1-5页。
- **核心逻辑：** 生命不是起源于难以复制的RNA，而是起源于容易自发产生的“小分子反应网络” 。

- **数学支撑：** 根据图论和相变理论，只要分子足够多，这种“集体自催化集”的涌现是数学上的必然（一阶相变） 。这是生命诞生的物理地基。

2. 三阶嵌套康德整体协同演化 (Evolution: 3rd-Order Nested Kantian Wholes)

- **对应内容：** 第6-8页。
- **核心逻辑：** 生命的升级方式是“套娃”。

    - **一阶：** 小分子集、肽集、RNA集独立存在。
    - **二阶：** 肽与RNA互助（协同进化），形成更复杂的整体。
    - **三阶：** 小分子代谢网被包裹进来，形成具备“代谢+遗传+酶”功能的原始细胞（原核生物）。

- **机制：** 自然选择作用于整体，部分（如RNA、肽）为了维持整体而存在。

3. 约束闭合热力学自主能动性 (Nature: Constraint Closure & Agency)

- **对应内容：** 第7、9页。
- **核心逻辑：** 什么是“活”的？
    - **约束闭合：** 细胞利用能量（爆炸）建造约束（大炮），约束又指导能量释放。细胞字面上是在“自我构建”。

    - **能动性：** 这种自我构建能力赋予了细胞“自主权”，让它能感知环境、判断好坏并采取行动。生命从此拥有了“意义”。

4. 减号：牛顿物理学预设相空间决定论 (- Newtonian Pre-stated Phase Space)

- **对应内容：** 第10页。
- **核心逻辑：** 为什么物理学推导不出生物学？
    - **颠覆性观点：** 牛顿和量子力学都要求预先设定所有可能发生的状态（相空间）。但生物演化（如进化出听觉）是在不断创造**全新**的可能性空间。

    - **结论：** 世界不是一个定理，生物圈是一个不可推导的、不断传播的构建过程。

下一步行动

既然文章内容已经全部分析完毕，根据您最初上传的 `画图逻辑.md` 要求：

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请问您现在需要我为您生成这张展示“生命起源与演化大统一理论”的核心思想示意图吗？

（如果需要，请回复“画图”或类似指令，我将启动图像生成工具，为您呈现一张包含自催化网络、康德整体套娃结构以及约束闭合循环的专业视觉图。）

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Is the emergence of life and of agency expected?

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We present an integrated and testable theory for the spontaneous emergence of life up to the prokaryote with template replication and coding. Collectively autocatalytic small-molecule sets, DNA sets, RNA sets and peptide sets have been discovered or created. Reliable theory supports the claim that such systems can emerge as a first-order phase transition. Such sets constitute Kantian wholes: the whole exists for and by means of the parts. We propose that the earliest life began with small-molecule collectively autocatalytic sets as first-order Kantian wholes. These merged with two other first-order Kantian wholes—peptide and RNA autocatalytic sets—to form a third-order Kantian whole. The autocatalytic, small-molecule set coevolved to become the metabolism of the entire system. The peptide and RNA collectively autocatalytic sets ultimately coevolved to template replication, coding and the ribosome. The same peptide–RNA coevolution may have broken chiral symmetry. Collectively autocatalytic sets achieve *constraint closure*. Thermodynamic work is the constrained release of energy into a few degrees of freedom. In constraint-closed systems, a set of boundary condition constraints on the release of energy, [A,B,C], constrains that release in a set of non-equilibrium processes, [1,2,3], to construct the very same set of boundary condition constraints, [A,B,C]. Cells literally construct specifically themselves. Because constraint-closed systems carry out thermodynamic work cycles, they constitute molecular autonomous agents that are able to sense, orient, decide and act in their worlds. These theories overlap and unite with the RNA world hypothesis.

This article is part of the theme issue 'Origins of life: the possible and the actual'.

1. Introduction

For the past four decades, the *RNA world hypothesis* has dominated work on the origin of life. Our purpose is to explore whether an alternative view, *collectively autocatalytic sets*, may now warrant serious research efforts. The two views may overlap in useful ways.

Robertson & Joyce [1] summarized the three central tenets of the RNA world hypothesis:

(i) at some time in the evolution of life, genetic continuity was assured by the replication of RNA;
(ii) Watson–Crick base pairing was the key to replication;
(iii) genetically encoded proteins were not involved as catalysts.

These authors point out that 'RNA World hypotheses differ about life that may have preceded the RNA World, about the metabolic complexity of the RNA World, and about the role of small molecule co-factors, possibly including peptides, in the chemistry of the RNA World' [1].

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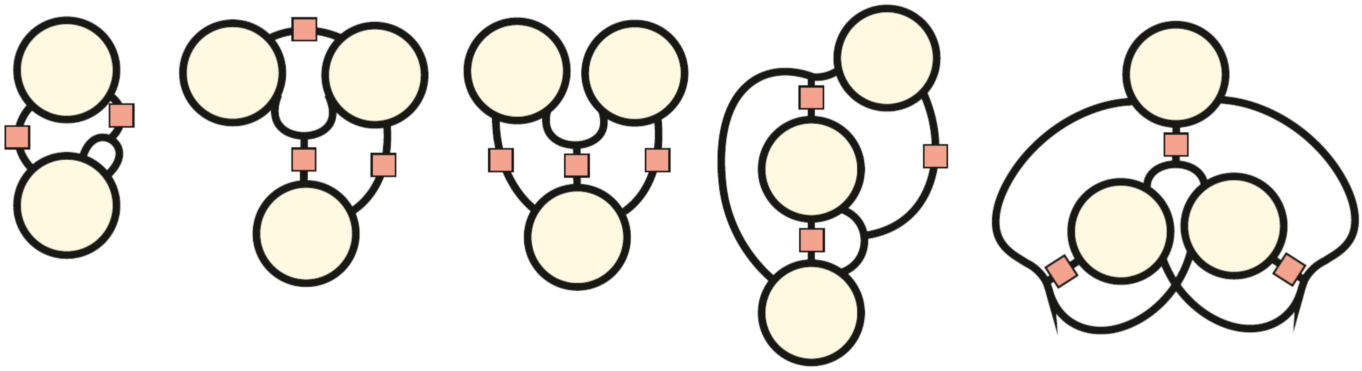

Figure 1. The five collectively autocatalytic motifs. Derived from [17].

Nobel Laureate Walter Gilbert proposed the RNA world hypothesis in 1986 [2]. Work over the years has focused on attempts to create template-replicating RNA or RNA-like polymers without enzymes [3–5]. Recently, Wachowius and Holliger, using *in vitro* evolution, have obtained an RNA sequence able to act as a polymerase and template to replicate several hundred nucleotides [6].

2. Metabolism first: collectively autocatalytic sets

The RNA world states its first tenet: 'Genetic continuity was assured by the replication of RNA'. It is of major importance that template replication is not the only chemical means to ensure continuity. Persistently reproducing collectively autocatalytic chemical reaction sets affords a different means for chemical reproduction and temporal continuity. Such systems have been proposed for five decades, and DNA, RNA, peptide and lipid collectively autocatalytic sets have been produced experimentally [7–16].

(a) Collectively autocatalytic systems without catalysts

We distinguish two senses of 'collective autocatalysis'. In the first, there are no 'catalysts', rather, reaction cycles themselves constitute the catalysts. In the other sense, there are catalysts in the system, as discussed below.

Consider a hypothetical open chemical reaction network: $A + B \rightarrow 2C$, $C + D \rightarrow 2E$, $E + F \rightarrow 2A$. There is a reaction cycle: $A \rightarrow C \rightarrow E \rightarrow A$. If A, C and E are initially in the reaction system, and B, D and/or F are supplied exogenously, the abundance of A, C and E will increase autocatalytically. The reaction cycle itself is the catalyst.

Recently, Nghe and collaborators have demonstrated that there are only five specific 'collectively autocatalytic motifs' [17] (see figure 1). These five motifs differ in their stability in open reaction systems, increasing from 1 to 5.

Increasing grounds exist to think that chemical reaction cycles are abundant in chemistry space [18]. Wolos and colleagues in 2020 studied 'Synthetic connectivity, emergence, and self-regeneration in the network of prebiotic chemistry' [18]. They report an abundance of chemical reaction cycles. These cycles are autocatalytic and hetero-catalytic. If each cycle can act as a catalyst, then mutually linked cycles can act as collectively autocatalytic sets where the cycles themselves are the catalysts.

(b) Collectively autocatalytic sets with catalysts

Figure 2 shows a simple hypothetical chemical autocatalytic set. Figure 3 shows Ashkenasy's nine-peptide collectively autocatalytic set [15].

As noted, collectively autocatalytic DNA, RNA, peptide and lipid systems have been studied for years [7–16]. Are these reasonable candidates for life? For the earliest life?

Earliest life. Perhaps the most powerful recent evidence that molecular reproduction can be based on collective autocatalysis is found in two papers [20,21]. The first [20] demonstrated small-molecule collectively autocatalytic sets with no DNA, RNA, protein or lipid polymers. These sets, each with several hundred small molecules and metals, were found in archaea and bacteria from before oxygen was present in the atmosphere. It is deeply interesting that the two small-molecule collectively autocatalytic sets have an intersection set of 175 small molecules and 172 reactions that is itself collectively autocatalytic. This suggests that the precursor to archaea and bacteria utilized this intersection autocatalytic set. If so, this precursor small-molecule collectively autocatalytic set diverged into the sets found in the archaea and in the bacteria. These sets became the basic metabolism of all subsequent life.

A second paper [21] has shown that all 6700 prokaryotes have small-molecule collectively autocatalytic sets. These sets range in size from a few dozen molecular species and reactions to a few hundred. Presumably, these evolved from the primordial intersection set between archaea and bacteria over 2 billion years ago. An important caveat is that these sets are identified computationally. It has not yet been demonstrated that they reproduce *in vitro* (see figure 4).

It now seems plausible, perhaps highly plausible, that such small-molecule collectively autocatalytic sets were the first form of 'life' in the Universe. Such sets typically form a number of amino acids and at least one nucleotide, ATP. In addition, via ATP and NAD, they couple the rudiments of the two major energy systems in living cells. Other sources of energy have been hypothesized as arising from wet–dry cycles [22], or from transmembrane proton and CO_2 gradients [23].

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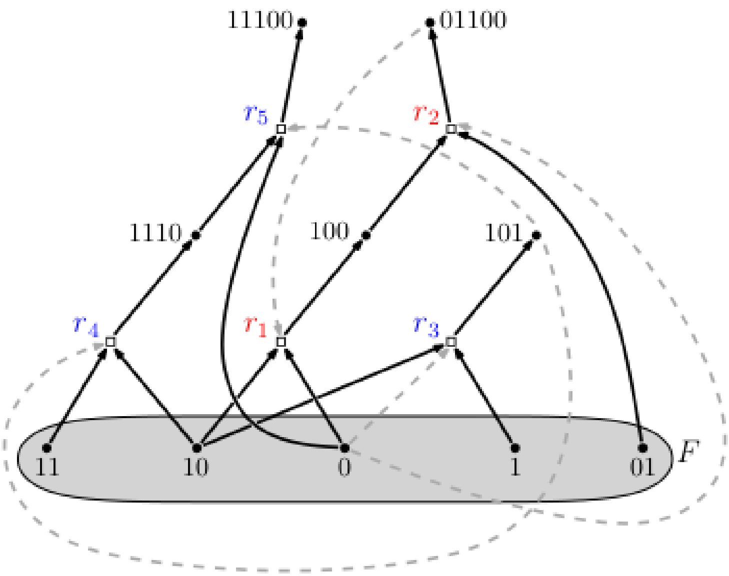

Figure 2. A simple collectively autocatalytic set. The model molecules are bit strings acting as substrates and products of reactions. Black solid arrows are drawn from the dots representing substrates of a reaction to a box representing the reaction. Black solid arrows are drawn from the reaction box to the dots representing the products of the reactions. The actual direction of flow of the reaction depends upon displacement from equilibrium. Dashed lines from dots representing molecules to the boxes representing reactions depict which molecules catalyse which reactions. The exogenously supplied food set of monomers and dimers is shown in the grey oval. Derived from [19].

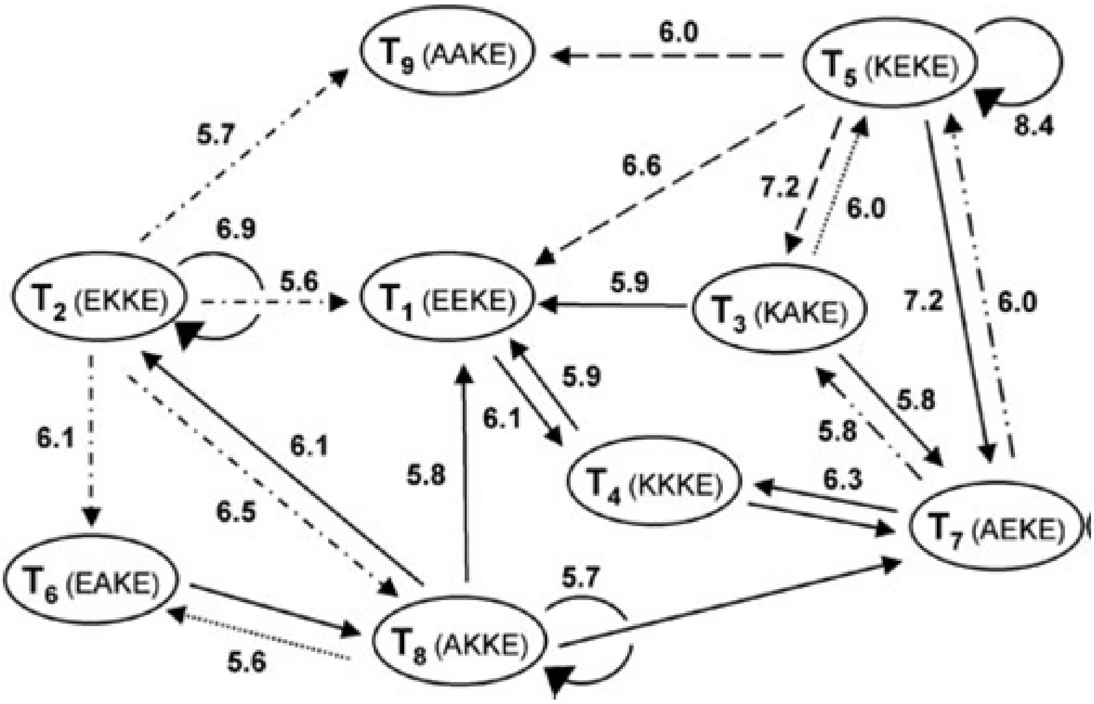

Figure 3. The nine-peptide collectively autocatalytic set discussed in [15]. The ovals show the molecules, and the arrows show the transitions among the molecules and the relative rates.

The existence of small-molecule collectively autocatalytic sets in all 6700 prokaryotes poses a serious challenge to the RNA world hypothesis in which continuity is always maintained by template-replicating molecules. To persist, any such template-replicating RNA would have had to acquire a connected chemical reaction network metabolism leading from simpler chemicals to the needed nucleotide building blocks of the RNA molecule itself, including U, A, C and G.

Here is the challenge: in any such metabolism that evolved to support the RNA template-replicating molecule, there is no reason to think that the metabolism itself would be collectively autocatalytic. On an RNA world hypothesis where continuity is assured by template replication (tenet () above) there is no need for the small-molecule metabolism to be collectively autocatalytic. And to function as a metabolism to support the replicating template, there is no reason for the metabolism itself to be collectively autocatalytic.

The RNA world hypothesis may not itself explain either the origin of life or what existed prior to an RNA world [1]. It seems an attractive hypothesis that small-molecule collectively autocatalytic sets were the earliest form of life on this, and perhaps all life-sustaining planets. This suggests a new union between the RNA world hypothesis and a collectively autocatalytic set view, where such a small-molecule set coevolves to become the metabolism of a later RNA or an RNA–peptide reproducing system.

Figure 4. A small-molecule collectively autocatalytic set with no DNA, RNA or peptide polymers in a prokaryote. Similar small-molecule autocatalytic sets are found in all 6700 prokaryotes. Presumably, the phylogeny among these is part of the evolution of metabolism. Derived from [20].

(c) The evolution of small-molecule autocatalytic sets

The early archaea and bacteria both have small-molecule collectively autocatalytic sets, with 394 and 292 molecules, respectively, and they share an intersection set of 175 small molecules and 172 reactions that is itself collectively autocatalytic [20]. As noted, presumably the intersection set evolved to the archaea and bacteria sets.

There are two major pathways for such small-molecule collectively autocatalytic sets to evolve:

(i) Collectively autocatalytic sets are typically comprised of one or more *irreducible collectively autocatalytic sets*. Such an irreducible set has the property that if any single reaction is removed from the set, the set is no longer collectively autocatalytic. Irreducible collectively autocatalytic sets, as replicators, can function somewhat as do genes [24]. Such an irreducible collectively autocatalytic set can transition from one to another larger collectively autocatalytic set, rather as do transposons today. Sets can evolve. We can study this evolution of metabolism computationally. It is NP-hard to identify all the irreducible collectively autocatalytic sets in a larger set [19]. However, it is possible to identify many such irreducible sets among those found in 6700 prokaryotes. Let *N* irreducible sets have been identified. Then each of the small-molecule collectively autocatalytic sets in any one of the 6700 prokaryotes has some specific members among the *N*. These can be identified. This should reveal patterns in the evolution of metabolism among the prokaryotes.

(ii) The presence of spontaneous reactions with the members of a small-molecule collectively autocatalytic set implies that spontaneous reactions can create small molecules that are not members of the current small-molecule collectively autocatalytic set [25]. If a novel product molecule is created by a spontaneous reaction, and if that product molecule or other molecules in the extant set can catalyse that spontaneous reaction, then the reaction and product molecule are added to the now enlarged small-molecule collectively autocatalytic set.

It may be technically possible to unite microfluidic systems and mass spectrographic instruments to analyse such metabolic evolution. Here, one injects a microvolume droplet of buffer containing a small-molecule collectively autocatalytic set into an oil microfluidic system that cycles the droplet. The droplet can be 'fed' by injecting further fluid containing desired input molecules. The droplet can be divided into two droplets that cycle further. One of the two droplets can be fed into a mass spectrograph system to analyse the small molecules in the droplet. The total system has become a flow reactor that can select for increased rates of autocatalysis, and it can also ascertain whether the system has expanded into its chemical adjacent possible. We can study the evolution of metabolisms.[1]

(d) The emergence of reproduction as a local fluctuation

We have considered two forms of collectively autocatalytic sets: those without catalysts, where the cyclic structures in the reaction networks constitute the catalysts, and collectively autocatalytic sets with true catalysts catalysing the reactions. These two may function together:

(i) Consider a complex reaction network with many autocatalytic and hetero-catalytic cycles. Because the reactions are autocatalytic and the systems are open, some of the members of these auto- and hetero-catalytic cycles may rise to concentrations far above their equilibrium concentrations [18].

(ii) Irreducible small-molecule collectively autocatalytic sets can be comprised of a modest number of molecular species [20,21]. Given high concentrations of some of the different molecules present among the auto- and hetero-catalytic reaction cycles in some locales, these might also happen to comprise at least one irreducible small-molecule collectively autocatalytic set.

(iii) Thus, small-molecule collectively autocatalytic sets might emerge as a local fluctuation. Once formed, such sets may then be able to evolve by exploring their chemical adjacent possible.

(iv) *Molecular reproduction at the level of small molecules could have arisen as a fluctuation.*

(e) The emergence of collectively autocatalytic polymer sets as a first-order phase transition

The possibility that self-reproducing collectively autocatalytic sets can arise as a *first-order phase transition* has been under investigation since 1971 [7–18,20,21]. Well-grounded theory has shown that in a system with an increasing diversity of molecular species of increasing molecular complexity, at some point a first-order phase transition is reached at which collectively autocatalytic sets spontaneously emerge [7–9,19,26]. Such a phase transition would be the emergence of molecular reproduction. The mathematics underlying this phase transition parallels the first-order phase transition in random graphs as the number of connections between a fixed set of vertices increases. Giant components connecting a large fraction of the vertices in a giant cluster suddenly emerge when the ratio of edges to vertices increases beyond 0.5.

With respect to collectively autocatalytic sets, we consider bipartite reaction graphs (see figures 3 and 5). Ovals represent molecules and boxes represent reactions. For each of the molecules and reactions, arrows run from substrate molecules into a reaction box. Arrows run from the reaction box to the product molecules. The directions of arrows do not reflect the direction of thermodynamic flow towards equilibrium.

As the diversity of molecules and atoms per molecule increases, the number of ways to synthesize each of these more complex molecules increases, thus the ratio of reactions, R, to molecules, M, R/M, increases. The analogue of the Erdős–Rényi random graph [27] arises by defining a parameter, P_{cat}, which determines the probability that any molecule catalyses any reaction. The theory randomly assigns, with probability P_{cat}, to each molecule and each reaction a 'catalytic arrow', running from the molecule to the reaction it catalyses. The system is now a hyper-bipartite graph.

For a fixed value of P_{cat}, as the number and complexity of molecules increase, so R/M increases, and a first-order phase transition arises at which a collectively autocatalytic set emerges [8,9,26]. This first-order phase transition to collectively autocatalytic sets persists if the distribution of 'who catalyzes what' is a power law, uniform or Gaussian [19,26]. The same transition occurs if candidate catalysts must have sub-sequences that 'recognize' candidate substrates [25].

Figure 5 shows an example of such an autocatalytic set, derived from [8].

Parallel artificial life theory supports the same results. Years ago, Walter Fontana created 'algorithmic chemistry' [28]. Fontana maintained 50 000 Lisp expressions in a model 'vat' on his computer. Fontana fed novel Lisp expressions into his vat, and randomly removed Lisp expressions from the vat to sustain the total number of Lisp expressions at 50 000. The system models a flow reactor. Lisp expressions can act on one another to produce new Lisp expressions. By maintaining a constant total number of Lisp expressions in the vat, the system selects for Lisp expressions that increase in abundance. Fontana found, first, Lisp expressions that copied themselves and took over the vat. Further, when he disallowed these and re-ran his experiments, Fontana reliably found the spontaneous emergence of collectively autocatalytic sets of Lisp expressions.

Very recently, Agüera y Arcas *et al.* have extended Fontana's work with eight different base languages. They found the same spontaneous emergence of collectively autocatalytic sets in seven of the eight [29].

A sensible summary of the theory over the past five decades is that the spontaneous emergence of collectively autocatalytic sets of polymers, RNA, peptides, lipids, or all three, as a first-order phase transition can be expected [7–16,19,25,26,28,29].

[1]Gonen Ashkenasy, Wim Hordijk, Stuart Kauffman, Niles Lehman, Sijbren Otto, and Philippe Nghe shared in 2011 a small CERN grant to pursue initial phases of these ideas.

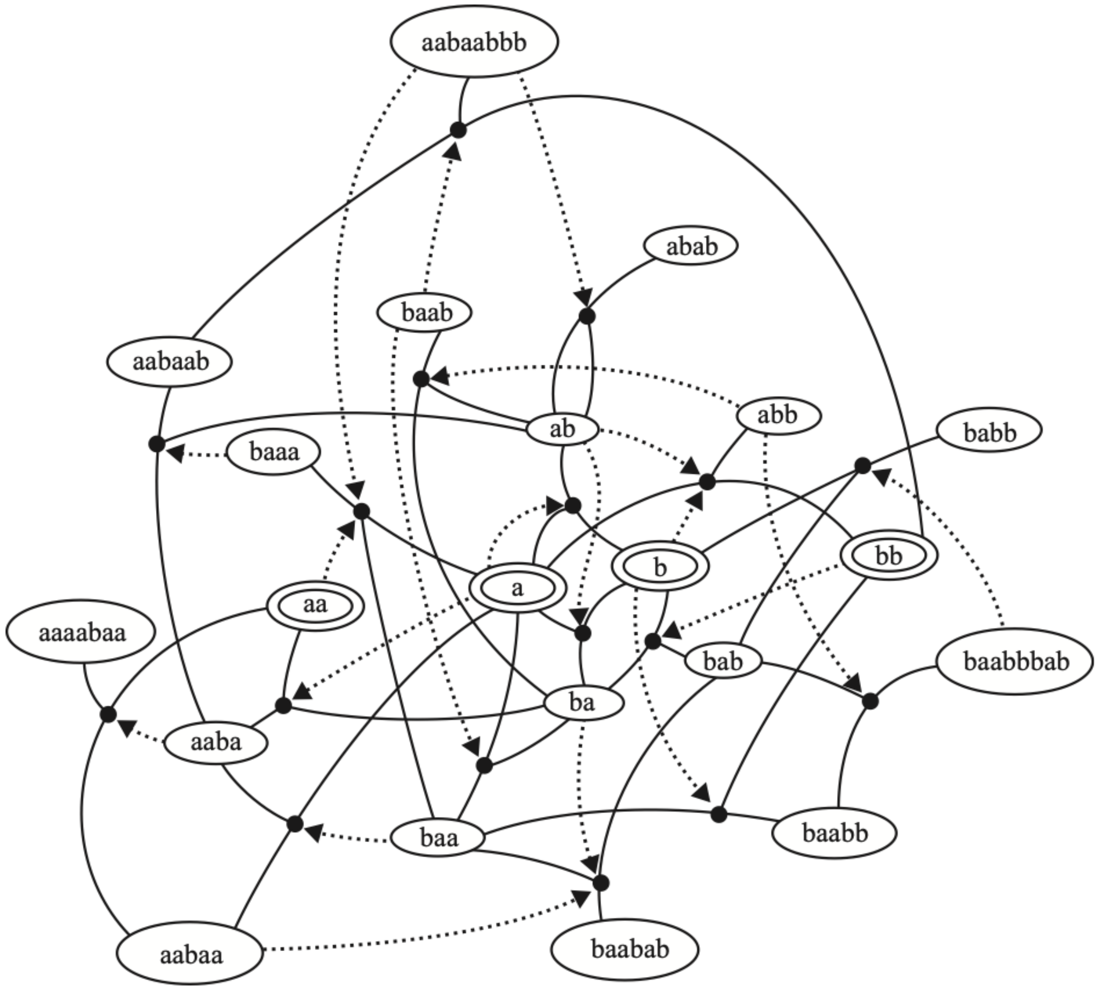

Figure 5. A collectively autocatalytic set of linear polymers derived from [9]. Ovals contain polymers of two monomer types, a and b. Allowed reactions, shown as dots, are cleavage and ligation reactions. A dotted arrow from a molecule oval to a reaction dot indicates that the molecule catalyses that reaction.

3. Experiments

If the above is true, and the abiotic universe generated complex molecular and polymer mixtures as found on the Murchison meteorite and elsewhere [30], life is expected, but the actual probability of its emergence and abundance in the Universe are yet to be calculated. More data are needed.

Experiments are needed. These all fundamentally ask: if the diversity and molecular complexity increase for some class of molecules, or mixture of classes, can we detect a phase transition emergence to collectively autocatalytic sets? Such experiments are now feasible. Eva Wollrab and Albrecht Ott [31], have run the Miller–Urey experiment for a month and generated thousands of small molecules as evidenced by mass spectrometry analysis. We now have the capability to generate highly diverse libraries of DNA, RNA and peptides [32]. It should therefore be possible now to test in detail whether collectively autocatalytic sets can emerge.

Macroscopic signatures of the emergence of collective autocatalysis would be highly valuable and may exist. Fontana's early results with algorithmic chemistry in a 'flow reactor' hints at one signature [28]. Fontana found that early in the process, the population of Lisp expressions was highly diverse but the copy number of each Lisp expression was low. After collectively autocatalytic sets emerged, the diversity of Lisp expressions dropped sharply and the copy number of each increased. This seems a macroscopic measure to test on a population of coevolving molecular species in a flow reactor maintained to enforce selection for molecules that increase in abundance faster than the flow exit rate from the reactor.

Agüera y Arcas *et al.* suggested that a higher-order entropic measure of the sequence complexity may be able to detect the transition to collective autocatalysis [29].

Assembly theory also supplies a means to assess whether a polymer sequence might be a sign of life [33]. Perhaps the same measure can detect the emergence of polymers in a collectively autocatalytic set and distinguish them from an earlier phase before collective autocatalysis has emerged in the flow reactor.

Beyond such signatures, detailed analysis will be required to assess which molecules catalyse which reaction in such sets to directly confirm collective autocatalysis.

If these experiments succeed with any single class of molecules, small molecules, peptides, RNA or with any mixtures of these classes, we will begin to have good evidence that molecular reproduction can, indeed, have emerged spontaneously in the Universe. Furthermore, for the first time, we will have the beginnings of quantitative data to assess the conditions for, and hence the probability of, such events in the Universe.

4. Breaking chiral symmetry

Chiral asymmetry in the molecules of life is famous. In encoded proteins, all amino acids are levorotatory (*L*). In polynucleotides in DNA and RNA, the nucleotides are all dextrorotatory (*D*). The fundamental question is why and how life's molecules broke chiral symmetry. There is no agreed answer ranging from the weak force to beyond [34].

A well-known theory by Frank in 1953 [35] proposes a form of autocatalysis. Given a racemic chemical reaction with *D* and *L* products, if the *D* products autocatalytically amplify the *D* version, chiral symmetry will be broken. The same holds if *L* products autocatalytically amplify *L*. Even more strongly, if the autocatalysis of *D* inhibits any autocatalysis of *L*, and *vice versa*, the system breaks symmetry either to all *D* or all *L*.

It is straightforward to generalize this basic idea to collectively autocatalytic sets of chiral polymers such as peptides or RNA. Assume a single testable postulate: homochiral polymers can function better as substrates, products and/or catalysts in reaction networks than can racemic polymers.

This postulate should be testable in racemic and homochiral polymers in collectively autocatalytic sets. For example, consider a homochiral all *L* peptide autocatalytic set. Substitute a modest fraction of the amino acids with *D* and test whether, under selection, the system returns to fully homochiral *L*.

The postulate above links collectively autocatalytic sets to the older theory from 1953. Each homochiral collectively autocatalytic set amplifies itself. In the presence of the other chirality, polymers that are all *L* and polymers that are all *D* amino acids will recombine by transpeptidation. This will yield racemic polymers that should be less efficient at any collective autocatalysis. Selection should yield the re-emergence of homochiral, or nearly homochiral autocatalytic sets. If confirmed, we would have a new basis to account for homochirality, with all *L* among encoded amino acids and all *D* among genetic polynucleotides. But the converse implication would be that collectively autocatalytic peptide sets and collectively autocatalytic RNA sets must have played a substantial role in the evolution of life on Earth. Such results would be consistent with the theory we develop here.

It is of considerable interest that a recent experiment demonstrates precisely the breaking of chiral symmetry and emergence of chiral molecules, 5-pyrimidyl alkanol, in a simple autocatalytic system [36].

5. Kantian wholes, catalytic closure, constraint closure and spatial closure

(a) Living organisms are open, thermodynamic, self-reproducing chemical reaction networks that are Kantian wholes that achieve catalytic closure, constraint closure and are spatially bounded, or enclosed, often by an enclosing lipid membrane.

(b) A *Kantian whole* [37] has the property that the parts exist (in the Universe) for and by means of the whole. You are a Kantian whole. You exist for and by means of your organs—heart and liver and genes. They exist for and by means of being parts of you, the whole.

(c) The molecules in living cells form collectively autocatalytic sets. Each molecule has at least one last step in its formation catalysed by some molecule in the set or in the set of molecules that constitute its exogenous 'food' [7–9,19,26,38]. This is clear in Ashkenasy's nine-peptide collectively autocatalytic set (see figure 3). This is catalytic closure [7–9,19,26,38]. (In reality, some reactions are spontaneous.)

(d) Living cells achieve a newly recognized and powerful property: *constraint closure*.

  (i) Thermodynamic work is the constrained release of energy into a few degrees of freedom [39]. A cannon with powder and a cannonball at its base is an example. The cannon is a boundary condition constraint on the release of energy. When the power explodes, it blasts the ball down the hollow bore of the cannon. Without a boundary condition constraint on the release of energy, no thermodynamic work can be done [39].

  (ii) Thermodynamic work can construct boundary condition entities that can serve as constraints. For example, thermodynamic work was used to construct the cannon [40].

  (iii) In a constraint-closed system [41–43], a set of non-equilibrium processes [1,2,3] and a set of boundary condition constraints [A,B,C] coordinate in such a way that the constraints [A,B,C] constrain the release of energy in the processes [1,2,3], such that the work done constructs the very same set of constraints [A,B,C]. For example, A constrains the release of energy in process 1 to construct a B. B constrains the release of energy in process 2 to construct a C. C constrains the release of energy in process 3 to construct an A. The system literally constructs itself by doing thermodynamic work to construct the boundary conditions that constrain the release of energy to construct the very same boundary conditions. This is entirely new. We construct our automobiles. These have organized constrained releases of energy that do work. Gas explodes, wheels turn. But automobiles do not construct their own constraints on the release of energy. Cells do. Living cells construct themselves [42,43]. Owing to constraint closure, living cells construct *specifically* themselves. The familiar distinction between hardware and software vanishes. Constraint closure is an aspect of classical physics. We have not had the concept before.

  (iv) The union of Kantian whole, catalytic and constraint closure constitutes the mysterious *elan vital* of Bergson [44], here rendered entirely non-mysterious.

6. The evolution of prokaryotes

Our aim in this section is to sketch a testable pathway from small-molecule, peptide and RNA collectively autocatalytic sets to the emergence of prokaryotes with template replication and encoded protein synthesis.

The concept of a Kantian whole has enormous power. Given the definition of a Kantian whole, we derive a non-circular definition of the *function* of a part in the whole. *The function of a part is that subset of its causal consequences that sustains the whole*. The function of your heart is to pump blood, not jiggle water in the pericardial sac.

Natural selection acts *directly* on the Kantian whole, and only *indirectly* on its sustaining parts as their functions may improve. Vertebrates with better hearts have more offspring who inherit the better hearts. There is no direct selection on the heart.

Kantian wholes can form *nested Kantian wholes*. Consider a prokaryotic cell to be a first-order Kantian whole. A eukaryotic cell with chloroplasts and mitochondria is a second-order Kantian whole containing the first-order chloroplast and mitochondrion Kantian wholes. A multi-celled organism is a third-order nested Kantian whole. We, with our gut microbiome, are a fourth-order nested Kantian whole. It is of interest to ask whether the entire biosphere is comprised of nested Kantian wholes.

Consider then, early life with three different first-order Kantian wholes: (i) small-molecule collectively autocatalytic sets, (ii) peptide collectively autocatalytic sets, (iii) RNA collectively autocatalytic sets.

Now consider the union of the small-molecule sets and the peptide sets, or of the small-molecule sets and the RNA sets. These each form second-order Kantian wholes. Selection will act directly on this new, *higher*-order Kantian whole and indirectly on its parts. Such selection at the level of the higher-order whole might well select for the coevolution of the autocatalytic small-molecule set to become the metabolism of the small-molecule–peptide set or the small-molecule–RNA set. An immediate advantage of the fact that the metabolism itself is already collectively autocatalytic is that the takeover of catalysis of some of the metabolic reactions by peptides or ribozymes can be piecemeal as the second-order set evolves. Each set helps the other.

A step further might well unite peptide and RNA autocatalytic sets. Autocatalytic RNA sets reproduce subexponentially owing to the difficulty in strand separation of the double-stranded RNA form [45,46]. But if the RNA Watson–Crick strands can each form one or more stem-loops, and if peptides can bind these stems, then the peptides help to destabilize the double-stranded RNA and so help the RNA autocatalytic set to reproduce exponentially. Conversely, if the Watson–Crick strands each have two stem-loops and two peptides bind the two loops of the Watson–Crick strand, then that strand is acting as a ligase to help form a peptide bond between the two peptides that are part of the autocatalytic peptide set [45,46]. The peptide and RNA autocatalytic sets can coevolve. If this can occur, *a new third-order Kantian whole emerges with a metabolic, peptide and RNA collectively autocatalytic system evolving. Selection now acts directly on the third-order Kantian whole, and indirectly on its metabolic, peptide and RNA parts*.

The framework just sketched sets the stage for a plausible pathway for the ultimate evolution of template replication and even coding. Such coevolving third-order nested Kantian wholes may have been evolutionarily stable for some time.

(a) Template replication

Consider our hypothetical protocell, a third-order Kantian whole embracing metabolic, peptide and RNA autocatalytic sets. Suppose that RNA replication arises by the replication of two or more independent RNA collectively autocatalytic sets. To be concrete, let the polymer lengths of the RNA in each of the two sets be 20 nucleotides. During this replication, the double-stranded form of each of the 20 nucleotide sequences is present and does not readily melt. Let the two 20-*mer*, double-stranded RNA sequences *transiently* stack 3′–5′ end to end. Let the stack fall apart to permit further replication of each of the two independent RNA autocatalytic sets. In this setting, consider that some RNA, or some peptide in the protocell, is able to template replicate all 20 of any one of the four 20-*mers*. This helps the later replication of the relevant RNA autocatalytic set [46].

The suggestion is that an RNA or peptide polymerase can evolve *piecemeal* to help the replication of the separate RNA autocatalytic sets. This affords a potential pathway to the later emergence of an RNA or protein polymerase. At such a stage, replication must transition from the reproduction of independent autocatalytic RNA sets to the replication of the entire RNA genome by the polymerase. Experiments here seem feasible.

(b) Coding

The same framework may afford a plausible pathway to the evolution of coding. Such a theory builds upon the above, plus the important fact that *L* amino acids bind their current *D* anti-codon [47,48]. Thus, just as above, selection for *L* peptides that help melt the double-stranded *D* RNA form can coevolve in the peptide–RNA collectively autocatalytic set if the double-stranded *D* RNA form has one or more stem-loops that the *L* amino acids or peptides prefer to bind. Conversely, if the *D* RNA strands have two stem-loops, each of which binds an *L* peptide of the collectively autocatalytic peptide set, that RNA acts as a ligase to help the peptide set. As discussed in detail elsewhere, this coevolution can lead to polypeptide–polynucleotide co-linearity, and from there to coding [45].

(c) Chiral asymmetry

But more: if *L* amino acids and peptides do *not* bind their *L* RNA anticodons, this hints that the co-evolution of peptide–RNA autocatalytic sets simultaneously broke the racemic symmetry among amino acids to *L*, and it also broke the racemic symmetry among nucleotides to *D*. Experiments seem feasible.

The same theory suggests that RNA stem-loops played a role in ligating pairs of peptides or an amino acid and a peptide. Such RNA stem-loop ribozymes may have been the precursors to the ribosome [45]. In parallel, such stem-loop ribozymes could have played a role in the evolution of the two classes of aminoacyl-transferases that charge transfer RNAs [45].

Our hope is that the body of theory and work outlined above sketches a testable pathway for the emergence and early evolution of life from small-molecule collectively autocatalytic sets to nested Kantian wholes comprised of small-molecule autocatalytic, RNA autocatalytic sets and peptide autocatalytic sets that then evolve to full prokaryotes with template replication, coding, and translation, as well as ribosome function. Many steps seem testable.

In a paper expanding upon Fontana's work described above, Szathmáry, as early as 1995 [49], discusses in detail the emergence and coevolution of collectively autocatalytic systems of different levels. Szathmáry also foresees these issues as testable. Long ago, T. Gánti also considered the coevolution of template-replicating RNA, a metabolism and a bounding lipid membrane [50].

The emergence of higher-order nested Kantian wholes where selection acts at the level of the highest-level whole, and the lower-level wholes are parts of the highest-level whole, describes all cases of the emergence of new units of reproduction, variation and selection. In their seminal book, *The major transitions in evolution* [51], John Maynard Smith and Eörs Szathmáry emphasize that these transitions all concern the emergence of higher-level units of reproduction, variation and selection. If our hypothesis is correct then the evolutionary process of the emergence of ever higher-level units of selection began with the four first-order Kantian wholes: small-molecule collectively autocatalytic sets, peptide collectively autocatalytic sets, RNA collectively autocatalytic sets and lipid autocatalytic sets.

7. The emergence of agency

Living cells not only construct themselves, but as open thermodynamic systems, they must 'eat' to survive. In general, cells can evolve to 'eat' because living cells are nonlinear, dynamical systems with complex dynamical behaviour that enables living cells, receiving inputs from their environment and acting on that environment, to sense and categorize their worlds, orient to relevant features of their worlds, evaluate these as 'good or bad for me' and act based on those evaluations. This is the basis of *agency and meaning*. Agency and meaning are immanent in evolving life. The *semantic meaning* is: 'I get to exist for a while'. The capacity to 'act' is immanent in the fact that living cells achieve constraint closure and do thermodynamic work to construct themselves. The same capacity enables cells to do thermodynamic work on their environment. A cell's action is embodied, enacted, embedded, extended and emotive [40,42,43,52,53].

Cells are molecular autonomous agents, able to reproduce, do one or more thermodynamic work cycles and make one or more decisions, good or bad for me [52,53]. The capacity to learn from the world, categorize it reliably and act reliably may be maximized if the cell, as a nonlinear dynamical system, is dynamically critical, poised at the edge of chaos [54,55]. Good evidence now demonstrates that the genetic networks of many eukaryotic cells are critical [56,57]. Such networks have many distinct dynamical attractors and basins of attraction. Transition among attractors is one means to 'make a decision'. It will be of interest to test whether Kantian whole autocatalytic sets can evolve to criticality.

8. The evolving biosphere is beyond the Newtonian paradigm

It is beyond the scope of this article to discuss what may be its most important point: powerful grounds exist to conclude that the evolution of the biosphere is beyond the Newtonian paradigm and cannot be deduced. We can use no mathematics based on set theory to do so. The evolving biosphere is a propagating, non-deducible construction, not an entailed deduction [42,43,58]. This claim, if true, is the pivot around which science must change. The science of Newton and quantum mechanics requires a prestated phase space for entailing law. The evolving biosphere progressively constructs an evolving phase space that cannot be deduced. The conditions for entailing law fail.

9. Conclusion

We have tried to present an integrated and testable theory for the spontaneous emergence of life up to the prokaryote with template replication and coding.

Our theory is based on the successive emergence of small-molecule, RNA and peptide collectively autocatalytic sets. Each is a Kantian whole. We propose that these unite to form a third-order nested Kantian whole in which the small-molecule set becomes the metabolism of the system, while the peptide–RNA sets ultimately evolve to template replication and coding. The same peptide–RNA coevolution may have broken chiral symmetry.

Reliable theory supports the claim that such systems can emerge as a first-order phase transition in sufficiently diverse chemical reaction networks. Alternatively, small-molecule collectively autocatalytic sets may have emerged as a local fluctuation and evolved further.

Collectively autocatalytic sets achieve *constraint closure*. Owing to constraint closure, living cells construct specifically themselves. The familiar distinction between hardware and software vanishes. Because constraint-closed systems carry out thermodynamic work cycles, they constitute molecular autonomous agents that are able to sense, orient, decide and act in their worlds. Agency, behaviour and perhaps mind, evolve. The evolution of the biosphere is a non-deducible propagating construction, not an entailed deduction. These theories may overlap with the RNA world hypothesis in useful ways.

Ethics. This work did not require ethical approval from a human subject or animal welfare committee.

Data accessibility. This article has no additional data.

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