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New Chemistry News

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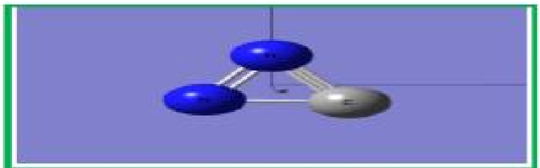
New News of Chem (NNC)



ChemNewsNew (CNN)

CNN – 37

Systems Chemistry (Syst.Chem., SC)-I

Information Source	ACS.org ; sciencedirect.com
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I. Object oriented terminology (OOT) for Syst.Chem

II. Select Research Titles(2000 to2020) in Syst.Chem

KLab
rsr.chem1979

I . Most-fascinating questions over the last hundred years

Life

- ? What is really (what we call) life
- ? Did life originate only onceby accident
- ?
  - ! Is it possible to define life scientifically in terms of strictly chemical and biological criteria
  - ! The principle "I know it when I see it''
    - ! Is not at all satisfactory with respect to life/Consciousness
- ?

- ? Where, When, How and from what did life emerge on our mother Earth
- ? Did life arrive here from some extra-terrestrial source instead
- ? Is it the probable outcome of chemical evolution, which has frequently occurred elsewhere in the universe

- ? Which property of living beings came first
  - ? Their ability to reproduce and transmit information to progeny
  - ? Their metabolic capacity
  - ? Their compartmentalization as individual entities

Conditions

- ? What are theset of sufficient conditions that could generate an ''organism''that we would agree to call it as ''living"
  - ? Chemists are less or at least no better equipped to answer than biologists, geologists, planetary scientists, computer scientists, or philosophers
  - ? Nontrivial problem in itself

Were the first living organisms based on autotrophic or heterotrophic metabolic cycles

- ? Were they mainly feeding from inorganic or organic materials

---

- ? Why the particular biochemical building blocks of life that we know today were selected
- ? How some of these biomolecules developed to have specific chirality

---

Another Life Elsewhere

- ! Life (carbon based as here) elsewhere (i.e.on other planets)
- ! Another type (with different base like photon, silicon etc.) here/elsewhere
- ! Other forms of life very different from those currently known to science now
  - ? Do they exist
  - ? If so, they are made of what
    - ? How to recognize
    - ? If recognized, what to do ;
      - ? How to make use ….exploit….
      - ? …….
- ! ~~~~~~~

Chemistry Life Chemistry

- ? How life's chemistry originated on Earth 4 billion years ago

- ? How it evolved over 1 billion years in the first phase
- ? How evolution over last ca 3 billion years resulted in homo sapiens (wise men)
- ? How last ca 100K years evolution finetuned homo sapiens into modern species with slow/little evolution rate

A grand challenge in today's science

Living species from chemical systems

Living systems	☞ Possible pathways for
	▪ Lifeless chemical soup (inanimate matter) →living systems
	
	☞ Transition of chemistry into biology
	+ Acquisition of function characteristics
	  + To replicate
	  + To metabolize
	  + To be spatially segregated from its environment
	  + Functional integration of all of these characteristic
	
	+ Active
	+ Dynamic
	+ Achieved sophisticated function
	  ! Life manages to stay far from equilibrium
	  ! Since equilibrium is death

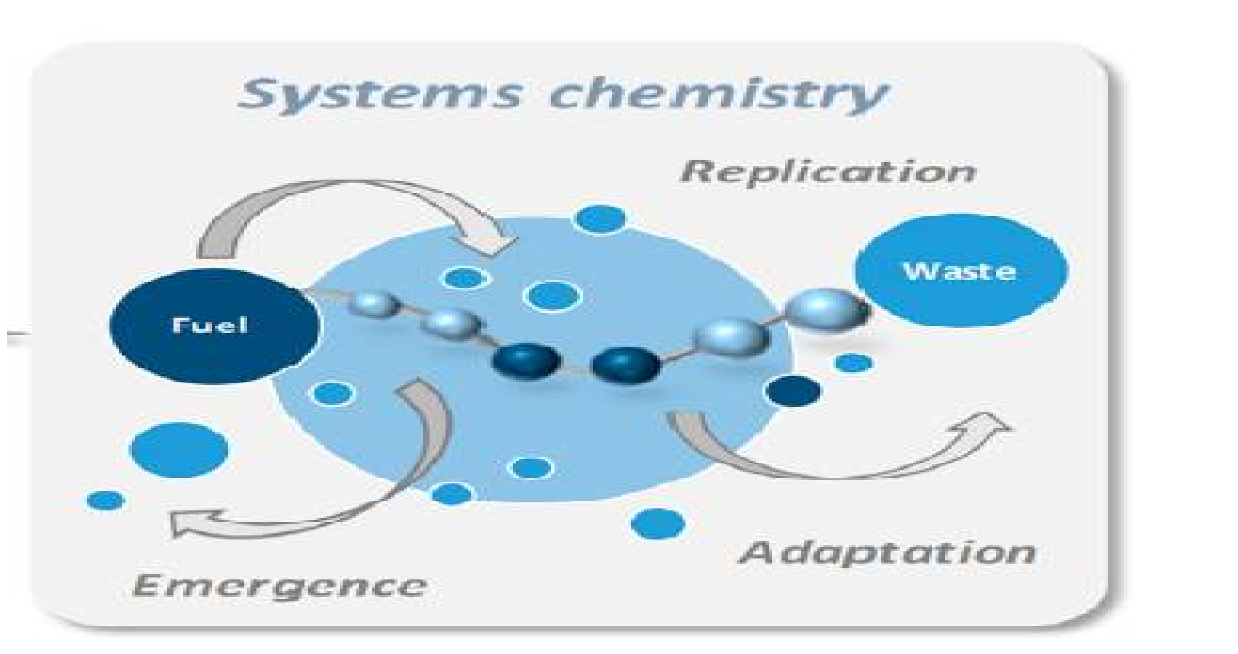
Complex Chemical systems inspiredby Living species

Man-made chemical systems	- Still less functional - Passive and static ! **Reason:** limited complexity and insufficient kinetic control

Complex chemistry in nature
Biosphere. Natural selection
☞ Giant molecular clouds in interstellar space. – natural selection does not apply ☞ Oceanand atmospheric chemistry
Biology
☞ Biochemistry of metabolic pathways
Fates of individual actors' networks determined by System as a whole Not just by the independentmerits of the actor itself

Systems Chemistry

Definition	Dynamic supersystem (chemical pendant)Integrating(in a Bottom-up approach) well-established branches of Science with an undercurrent of chemistry		
	o Pre-biotic/supramolecular chemistry o Theoretical chemistry o Autocatalysis	o Theoretical biology	o Computer Science o Complex Systems



Inspiration	🕭 System Biology; System Analysis 🕭 Simple Chemical Blocks 🕭 Synthetic Biology 🕭 BioBricks50 → to develop functional biological circuits from standardized parts
Goal	☞ Origin and synthesis of life
	- What is achievable with systems chemistry is limited by the creativity of the chemist

	☞ Development of complex synthetic systems displaying emergent properties
Aims/objectives	☞ To develop experimental/ theoretical frameworkswithin systems chemistry approach ☞ Holistic study of mixtures of simpler chemical components (as building blocks) in pre-biotic environment for very long period !

Aims/objectives	☞ To explore/understand how interactions give rise to unexpected, novel and useful properties ! Characteristic only of the systems as a whole Cannot be traced back to an individual component ☞ Systems chemistry follows a bottom-up strategy by ! i.e. complex systems are assembled from simple components ☞ To explore the chemical space of appropriate initial conditions ☞ Energy supplies for chemical mixtures to maintain a dynamic state of chemical substances thatspontaneously grow in numbers as time goes by

Aims/objectives	☞ To capture the complexity and emergent phenomena prevalent in the life sciences within a wholly synthetic chemical framework ☞ Unveil complex reactions networks ☞ Building minimal complex systems from their elementary components in a bottom-up approach ☞ To develop new functional materialswith enhanced physical properties ☞ To design systems with specific properties and functions from novel, minimalistic buildingblocks

Subfields	o Dynamic combinatorial chemistry o Oscillating reactions o Self-replicating networks o Chemical networks in compartments o High-throughput biochemical analysis o Microfluidics o In vitro evolution systems

Salient features

Equilibrium

- Continuously maintaining chemical systems away (or far-off)from thermodynamic equilibrium
- Pushing replication chemistry away from equilibrium

Networks

- Design and analysis of replication networks far from chemical equilibrium
- Compartmentalised chemical networks
- Incorporating feedback loops
- Chemically fuelled molecular motion
- Designed oscillators creating concurrent formation–destruction system

Kinetics

- Kinetic stability
- Self-assembly
- Design of self-synthesizing materials

Evolution

- Controlling supramolecular interactions
- Open-ended evolution with synthetic replicators
- Coupling/ integrating individual subsystems at various levels

Tools. Systems Chemistry

- Out-of-equilibrium systems
- Feedback loops

- Communication between
  - Components in multicomponent systems
  - Analysis of materials on different scales

- Chemical descriptors
- Upcoming integration of heterogeneous Knowledge of chemical biology
- Polypharmacology
- Clinical information

Additional tools. Systems Chemistry

- Systems chemistryalone is not sufficient for everything

Remedy: Forces operating in addition to chemistry(playing crucial roles)

- ☞ Mechanical forces
- ☞ External electromagnetic fields
- ☞ Phase separation
- ☞ Different modes of transport
  - o Diffusion
  - o Convection
  - o Osmosis— gradients

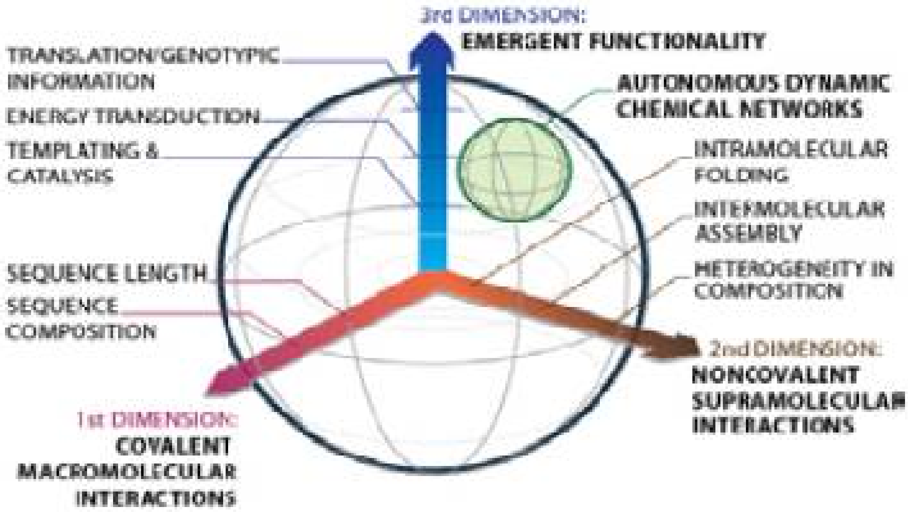
Challenges for Tools

- o Minimum human intervention after initiation
- o Technical novelty compared to traditional approaches in chemistry
- o Analytical handling of complex mixtures without separation
- o
- o Deep understanding of origins of biological complexity
  - o Sought-for next “quantum leap”
  - o To generate self-evolving properties → self-evolving behavior

! The “Holy Grail” is to create new (??) life from inert matter

Outcome	Examples: Macroscopic emergent behaviors like ☞ Global warming ; climate change ☞ Trending phenomena on social networks ☞ Stock market crashes ☞ Feedback loops in predator populations

Emergent properties	☞ Output of complex chemical systems ☞ Result from the interactions between components of chemical networks assembled from the many predesigned components ☞ Unprecedented properties unique to these complex entities ☞ Properties that go beyond the sum of the characteristics of the individual constituents of the system ☞ Cannotbe attributed to any of these individual components acting in isolation



Timeline. Systems Chemistry

1986	Günter von Kiedrowski	o First experimental discovery of Autocatalytic self-replication of a self-complementary hexadeoxyribonucleotide
2005	Günter von Kiedrowski	o “Systems chemistry” term inventor o Described kinetic and computational analysis of a nearly exponential organic replicators
1927–2007	Leslie Eleazer Orgel	o Prophet

Conferences		
First workshop, Venice	2005	Workshop
Chembiogenesis	2005	Conference
EU research network on systems chemistry	2007	
Systems Chemistry + Chembiogenesis	2008	Maratea, Italy
Systems Chemistry II: + Evolution and Systems + Chembiogenesis	2009	Balatonfüred Hungary
Systems Chemistry III + Chembiogenesis	2011	

Centre	
2009	Centre for Systems Chemistry started at University of Groningen, Netherlands

Journals	
2010-2018.6	Open access Journal of Systems Chemistry launched ((von Kiedrowski et al.)through Chemistry Central platform now part of the Springer publishing house.
2019	ChemSystemsChem, Wiley online journal

Thermodynamics Kinetics | **Chemical process (es)** | **Nature** | **Man-made systems**

If	Non-living (inanimate matter) systems
Then	Thermodynamic considerations dominate & Kinetics remain playing secondary role
If	Living systems
Then	Kinetic state of matter matters & Do not tend towards equilibrium i.e. Maintain a far-from-equilibrium state by continuous exploitation of an external energy source

	Complex chemical systems-- thermodynamic models
If	A minimum energy state is reached
Then	Systems are under thermodynamic control
If	Propelled by continuous energy input
Then	Systems sustained far-from-equilibrium
If	Out-of-equilibrium networks
Then	Exhibit unique functions Examples: ▪ Selective information storage and propagation ▪ Molecular oscillation Fuelled unidirectional macromolecular motions
If	Trapped in local kinetic minima or driven by irreversible biological processes
Then	Systems are under kinetic control
If	Reaction networks involves kinetic feedback loops
Then	They outcome exhibits adaptive behaviours

kinetically trapped System	☞ In a local thermodynamic minimum Or ☞ Far-from-equilibrium state Or ☞ Reside in a metastable state

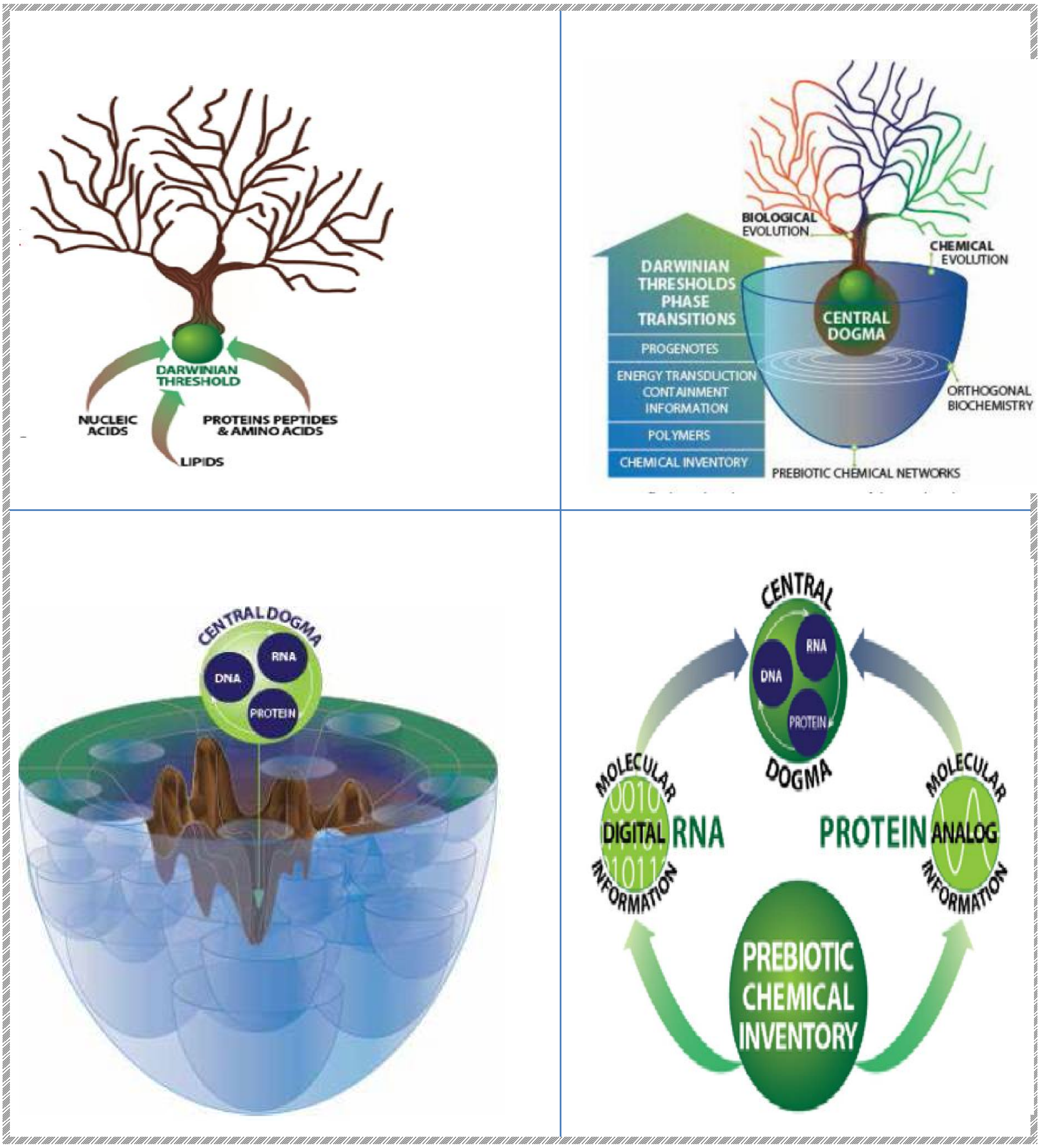
	- Maintenance requires continuous input of fuel
Kinetic control in the scope of systems chemistry	☞ Pseudo-dynamic combinatorial libraries ☞ Autocatalytic reactions ☞ Self-sorting processes ☞ Oscillating reactions ☞ Self-replicating systems ☞ Dynamic molecular networks ☞ Self-assembly networks of autocatalytic and replicating compounds ☞ Self-replicating systems with dynamic molecular networks and self-assembly

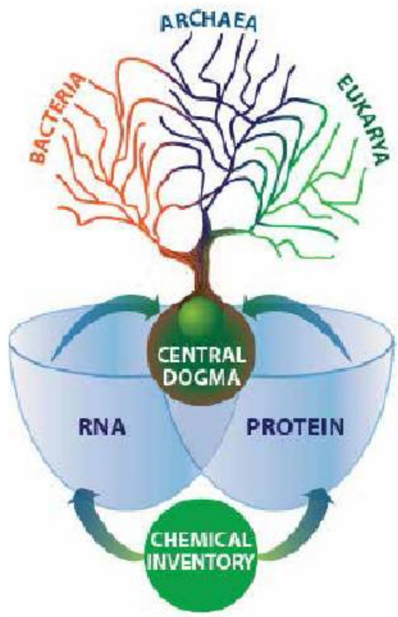
Experimental work on systems chemistry	Comprises of o Dynamic combinatorial libraries o Oscillating reactions o Replicating networks o Self-assembling systems

Life	☞ Incredibly complex functional molecular system
	☞ Comprises of complex, heterogeneous, massively parallel molecular reactions/ interactions ☞ That take place in non-equilibrium, dissipative conditions→ ! Connections and interactions give rise to a highly dynamic and functional whole

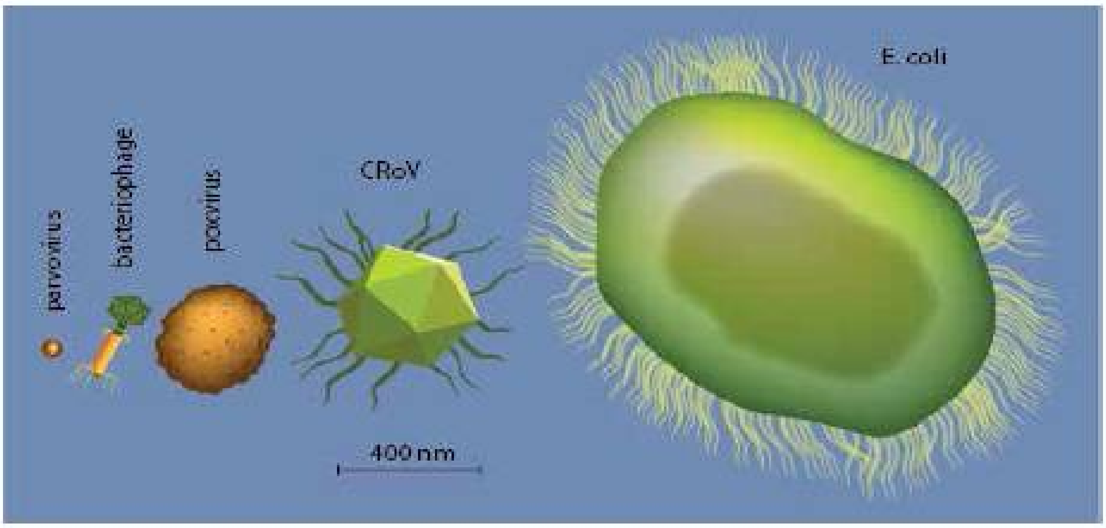
Physics / Chemistry/ biology of Life

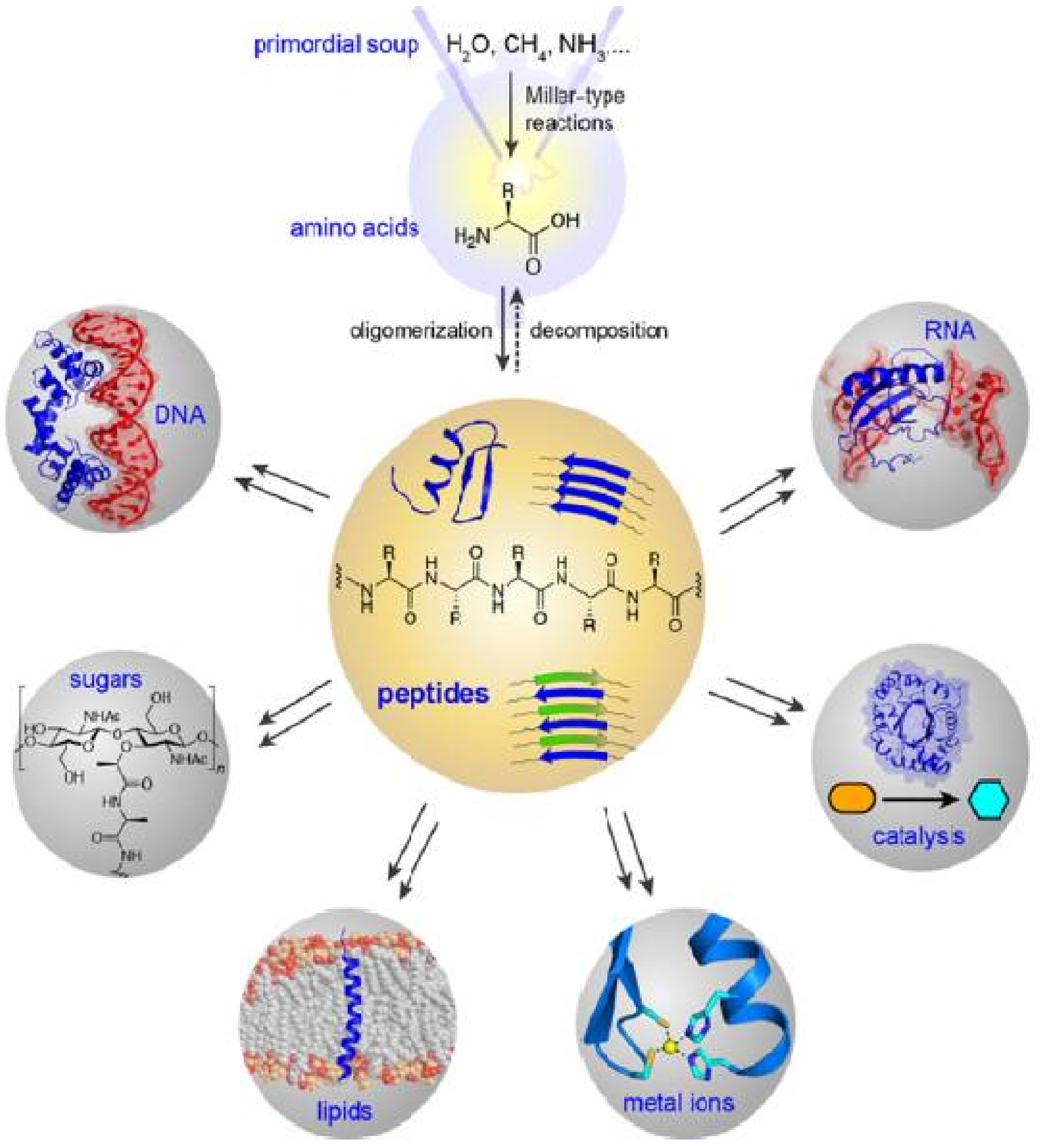
Pre-biotic era	☞ Approximately 3 billion year ago ☞ What was going on earth surface, ocean bed or up in the surrounding atmosphere for a period of over one billion years -- - Correct mapping untrusty





Living organism	☞ Mainly composed of water and organic molecules ☞ Molecular mechanisms that are much more diverse, complex ☞ Based on quasi-equilibrium structures extrapolating extant biological complexity backwards to ca 4 billion years (in time) into simple chemical transformations - Misleading





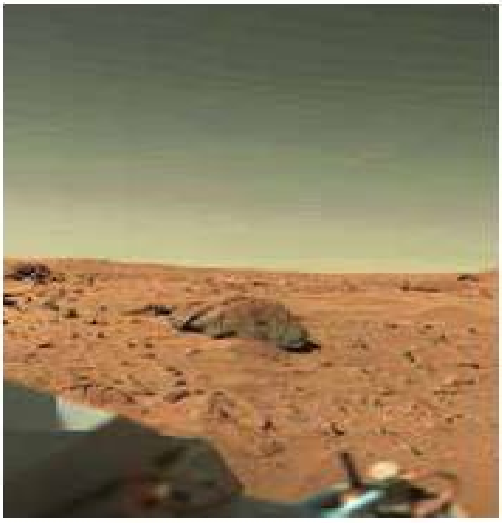
Primordial soup to bio-molecules in Extant life

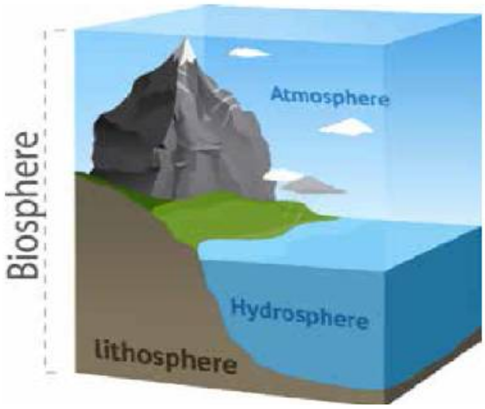
	☞ combine self-organization and self-assembly processes keeping many of the resulting molecular ensembles (i.e., polymers, membranes, etc.)
Life operates	☞ Far from equilibrium ☞ Kinetically controlled networks have greater relevance to biology ☞ What most researchers agree upon is that a combination of thermodynamic and kinetic processes

Life operates	Autonomous entities with the capacity for open-ended evolution ☞ Stability to process ☞ Transmits heritable information to progeny (i.e., a genetic mechanism); ☞ Ability to capture energy and material resources ☞ Staying away from thermodynamic equilibrium (i.e., metabolic machinery); ☞ ☞ Ability to keep its components together ☞ Distinguish itself from the environment (i.e., cell membrane).

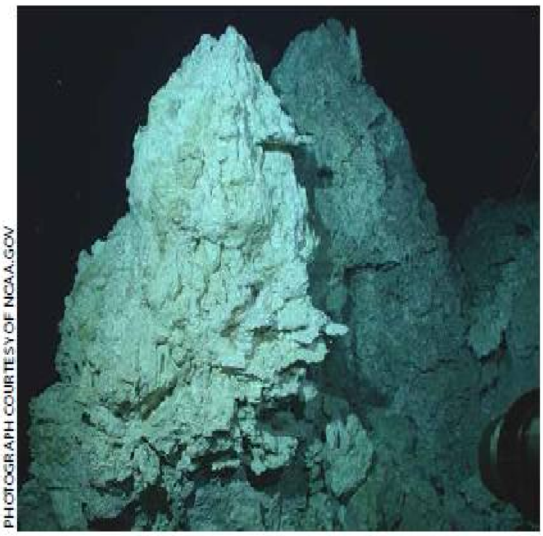
Dynamic combinatorial libraries (DCLs)	☞ Molecular networks where network members exchange building blocks ☞ Distribution of resulting product is under thermodynamic control ☞ Addition of a guest or template molecule shifts ☞ The equilibrium towards compounds that are receptors for the guest

Dynamic combinatorial chemistry (DCC)	Powerful approach o To create complex synthetic chemical systems o Response of mixtures to external stimuli o For exploration of functionality o For similarity assessment o Identification of new receptors not trivial through rational design
DCC	Complexity can be enriched with more o Types of reversible reactions o Complexed environments
Thermodynamically controlled DCC	☞ Energy surfaces connecting the different local minima are shallow ☞ Easily traversed





PHOTOGRAPH COURTESY OF NCAA.GOV



Looking beyond Known Environments

Recent advances	Spontaneous synchronization of oscillating reactions New methodology for developing chemical systems exhibiting reaction-diffusion patterns Chiral symmetry breaking in dispersions of crystals Emergence of self replicators from molecular networks Self-assembly under kinetic control Ex: Stoddart's Borromean rings (beautiful symmetric structures)

Chemical replicator system	Is still thermodynamically driven system Implies reaction will continue only until the equilibrium concentrations of the replicating molecule and its building blocks are reached
Living self-replicating chemical systems	High kinetic stability Keep far from equilibrium →Implies thermodynamically unstable

Applications. Systems Chemistry	
Drug discovery	o Intensive acceleration of o Pharmaceutical development

Materials Science	To design new functions complementary to those present in Nature o Smart materials o Catalysts Materials with life-like characteristics
Model synthetic systems	With properties that could reflect aspects of prebiotic biogenesis Developmentof replicators and self-assembling membranes

Trans-disciplinary research	→ To synthesizeinterface between supramolecular chemistry and biology

To explain	☞ What made transformation of a complex mixture of chemical compounds on prebiotic Earth into a life (living chemical system) possible ☞ Why the particular biochemical building blocks of life that we know today were selected ☞ How some of these biomolecules developed to have specific chirality? ☞ How emergent function arises in synthetic, simplified mixtures obtained through bottom-up approaches

Prospects.Systems Chemistry

Systems Chemistry as a tool

Origin of life

- ☞ To probe into chemistry→ to → biological molecules →to → life
- ☞ To go back from extant biology (i.e.today's human visual reality) →to → pre biotic primordial chemical world
  - ☞ Reduces gap between life's chemistry, complex chemistry and system's chemistry

De novo synthesis of life

- ☞ Systematically study how simple biomolecules interact to give rise to novel functions

Chemical factories

- o Self-synthesizing
- o Self-repairing

- Binding by a single receptor will provide only very limited information,
  - ✓ **Remedy:** More comprehensive description of the molecular structure using a systems chemistry

Origins of life-theories

- ☞ Traditional dichotomy of metabolism-first and gene-first
  - Can be quite misleading because both theories appear to be too ‘‘kinetically fragile’’ in that they easily revert to a thermodynamic minimum

Remedy:a systems-level approach

- ✓ Both metabolism and information transfer evolved roughly simultaneously
- ✓ Evolution of cellular boundaries that prevented dilution of this reactive far-from-equilibrium

Complex Systems Analysis + Chemistry+ Life→ Systems_Chemistry

Chemical world ~~~~~ Life .... Evolution Extant Biology...

<table>
<tr><th colspan="3">Non-life to Life</th></tr>
<tr><td>Formation atoms</td><td colspan="2">o Hydrogen, Carbon, Nitrogen, Oxygen, Phosphorus, Sulfur</td></tr>
<tr><td>Prebiotic soup</td><td colspan="2">o Hot dilute soup of organic substances for oceanic water containing mixture of simple organic compounds.</td></tr>
<tr><td>Abiotic</td><td colspan="2">o Synthesis of monomers, oligomers, and supramolecular systems</td></tr>
<tr><td>Organic/inorganic compounds</td><td colspan="2">o Methane (CH_4) was probably the first organic compound
o Hydrogen cyanide (HCN)was formed later
o Water (H_2O)</td></tr>
<tr><td>Formation of complex organic molecules</td><td>
<table>
<tr><th colspan="2">Prebiotic Synthesis</th></tr>
<tr><td>Monomers:</td><td>Lipids
Amino Acids
Nucleotides</td></tr>
<tr><td>Polymers:</td><td>Peptides,Proteins
RNA; DNA</td></tr>
<tr><td>Coevolution</td><td>Synthesis ofNucleic Acid</td></tr>
<tr><td>Chirality</td><td>Homochirality</td></tr>
</table>
</td><td>
<table>
<tr><th>$$$ World</th></tr>
<tr><td>Protein
Lipid (high-probability)
RNA (low probability)
DNA</td></tr>
</table>
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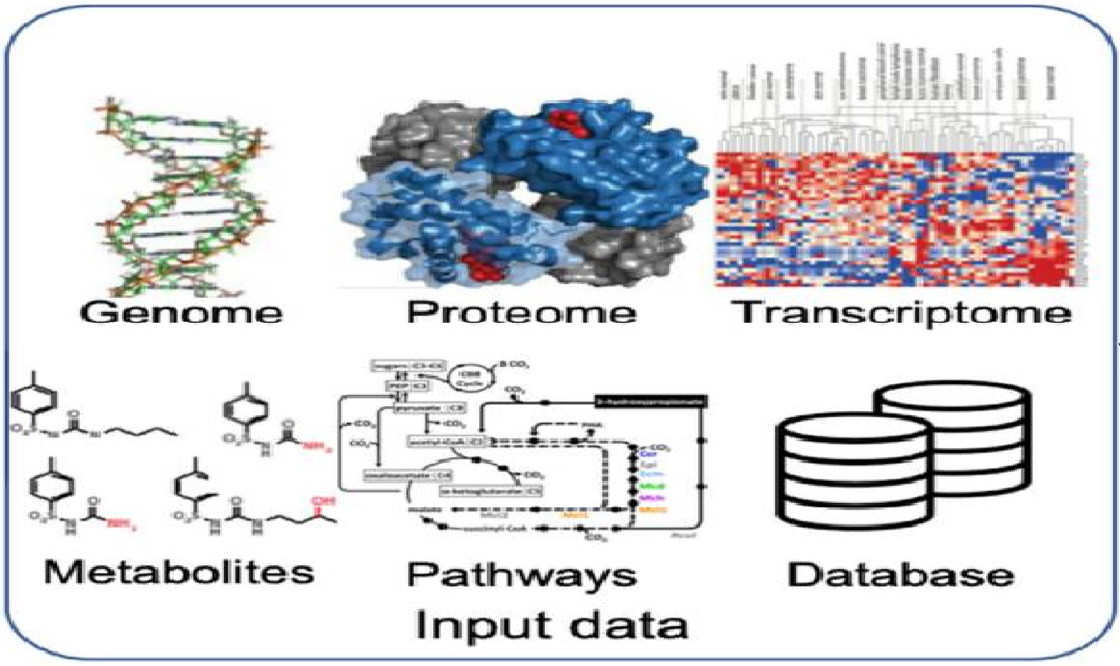
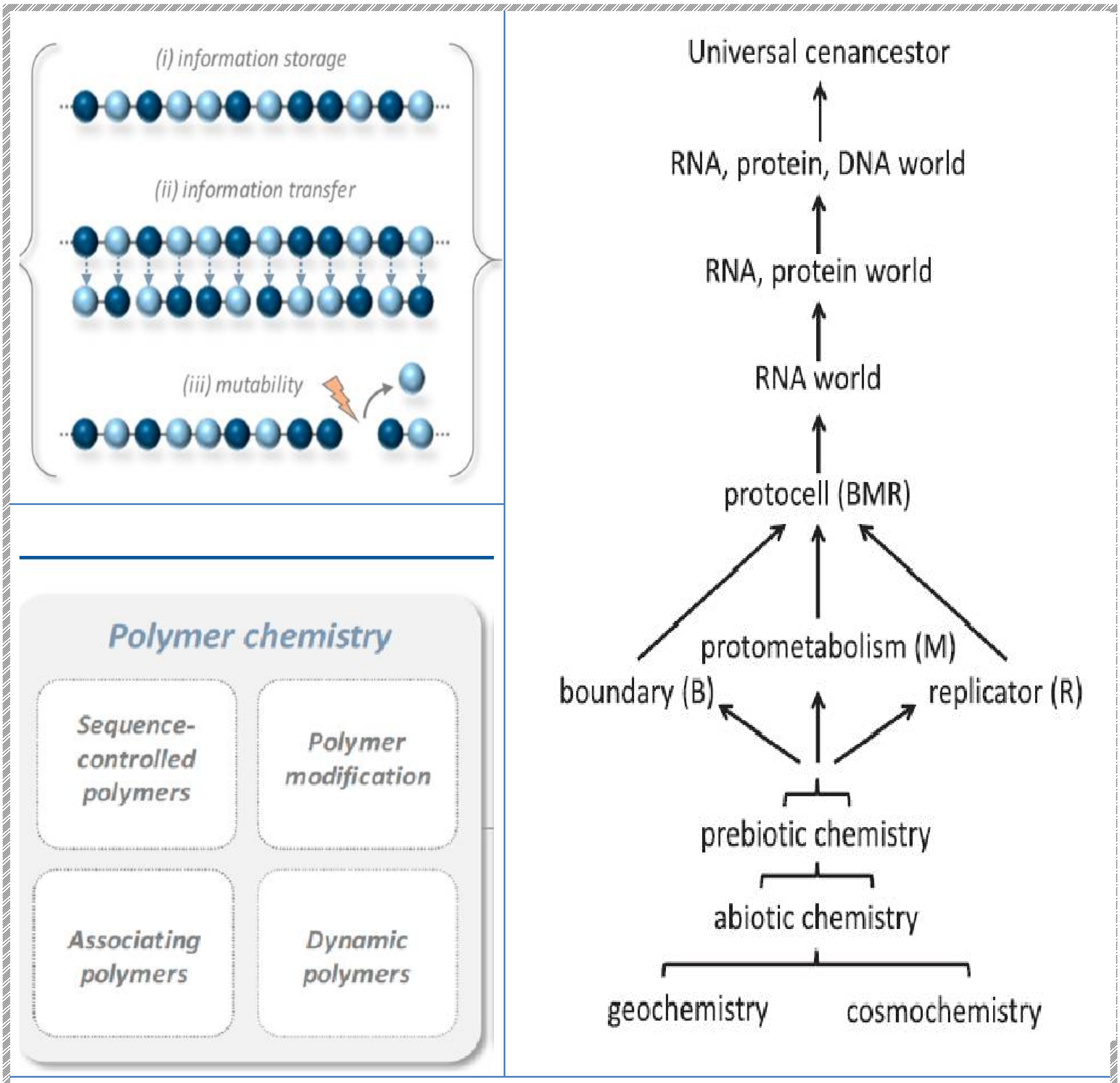
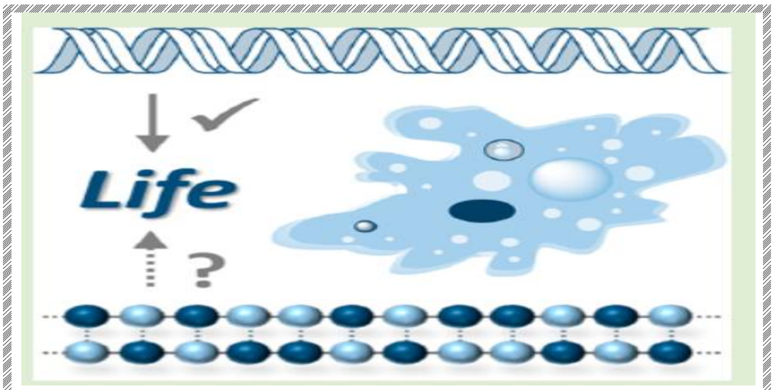




Simple chemical molecules to life’s machinary



Non-life chemicalsto lively life

Cooperative interactionsat a system level	☞ Functional cooperation and coevolution among these diverse classes of molecules from the earliest times

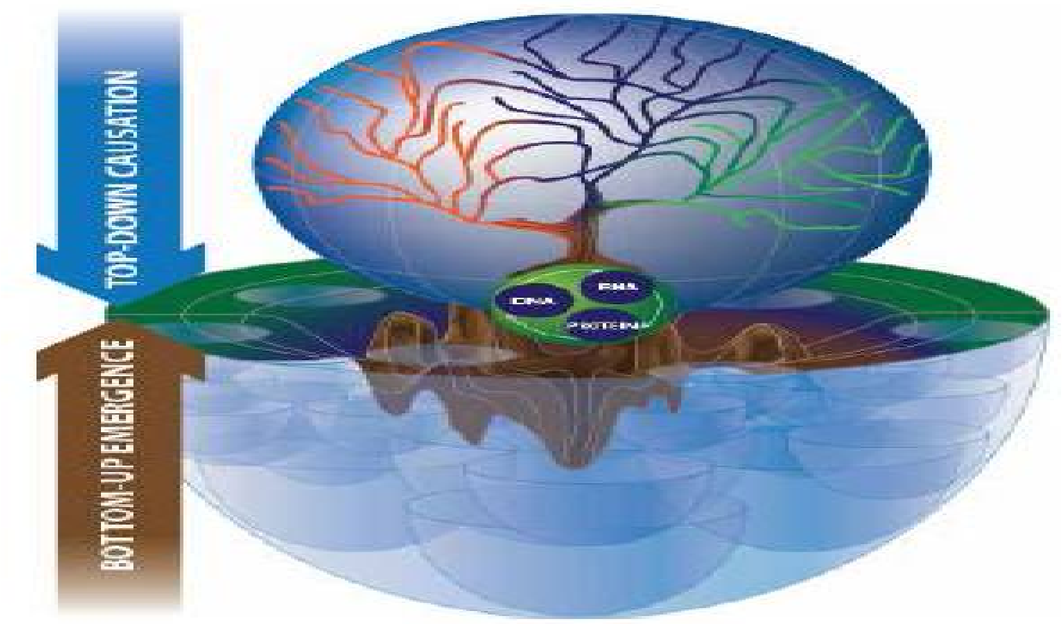
Prebiotic synthesis	☞ Amphiphiles
	☞ Total synthesis of racemic and enantiopure phospholipids
	☞ Evolvable molecular systems
	  ☞ Synthesis of fluorescent clickable probes
	  ☞ Synthesis of glycolipids

Life	Emergence of the first living entities

Chemistry of life	☞ Relies on biopolymers (proteins, nucleic acids) folding into specific conformations that dictate their properties ☞ Complex folded structures encountered in biology are the result of millions ofyears of evolution
Origin of life model	? Seek to replicate extant biochemistry (e.g., in alkaline hydrothermal vents) or ? To create the moleculesof life by using more traditional synthetic chemistry

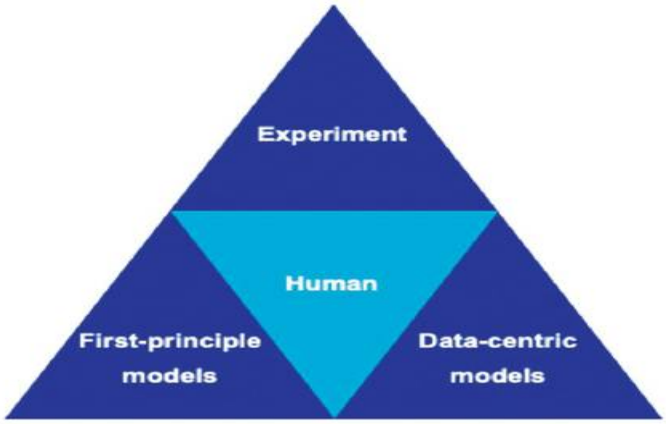
Foreseeable Future. Systems Chemistry	
Next generation	🔔 Chemists (The systems chemists) 🔔 Tools 🔔 Theories, Models 🔔 Pragmatic module
	Systems chemistry researchers + Interdisciplinary expertise + Trans-disciplinary working knowledge + Grasp of rare/ cutting edge technologies + Open-minded approach

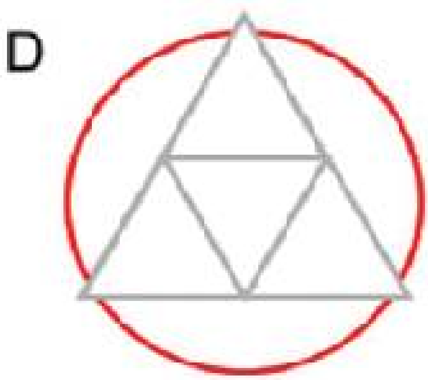
Tools	▪ Working with strict ‘‘bottom-up’’ designs ▪ i.e., avoiding recurrent viz. use of enzymes or other complex biomolecules ▪ ‘‘Top down’’ approach ▪ Viz. combinations of functional components that should integrate those intermediate - Many of these hypothesis-driven attempts will unfortunately fail Repetition with refined blue-print



Top-down and bottom-up approaches for non-life chemistry and life's chemistry

5^{th} Paradigm





Cognitive computing

- Natural language processing
- Knowledge representation
- Automated reasoning

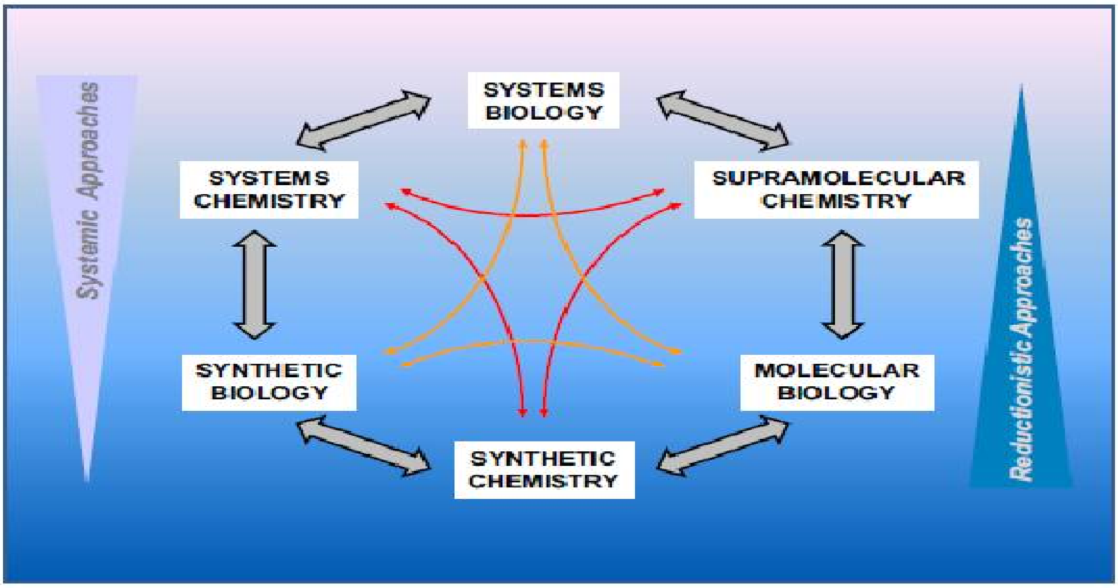
Models

- Data driven
- Model driven
- Empirical/ Stochastic
- Theoretical

Data
Numerical
Boolean
Literal
	Numerical
	o Integer
	o Floating point
	  - Real
	  - Complex
	  - Quaternion
	  - Octonion
		Data Acquisition
		- Experimental design
		DataMassaging
		- Data/ variable transformation
		- Noise filtering
		- Clustering/classification/Pattern recognition
		- Optimization (local, global, Pareto)

Paradigm	Tools
1^{st}	Human observation of natural world
2^{nd}	Directed experimentation
3^{rd}	In silico testing
4^{th}	Data-centric models
5^{th}	Cognitive computing

Open mind	Start Cycle ….. Test→ Failure → redesign → Failure ……… Near success Refine Go back to cycle
Future goals	- Preliminary road-map - Extant life - Artificial life supporting modules
Target	- Extending today's creativity from isolated molecules to molecular networks → ! New molecular systems with unique and exciting properties Approaches to characterizing individual building blocks utilized in living systems
Challenge	? To find the right initial conditions for system, of course, supplying it with energyvery often such that ! system prevails "on its own" - for a maximally long period of time



Systems approach to chemistry, biochemistry and life in nature and in man-made-artificial world

Outcome	! New design rules ! Design emergent behaviour

	▪ Synthetic systems
	  o Design of artificial cells
	▪ Capture many of the individual characteristics of life
	  o Compartmentalization
	  o Replication
	  o Metabolism
	▪ Integration under far-from-equilibrium conditions
	▪ Pareto-optimality – Thermodynamic & Kinetic stability
	▪ De novo synthesis of life
	▪ Process of manufacturing of chemicals
	  ✓ Nano- or microscale self-synthesizing tools of future
	  ✓ Energy efficient and clean chemical factories
	  ✓ Capable of regulating and repairing themselves

Today	- StillSystems Chemistry is in its infancy

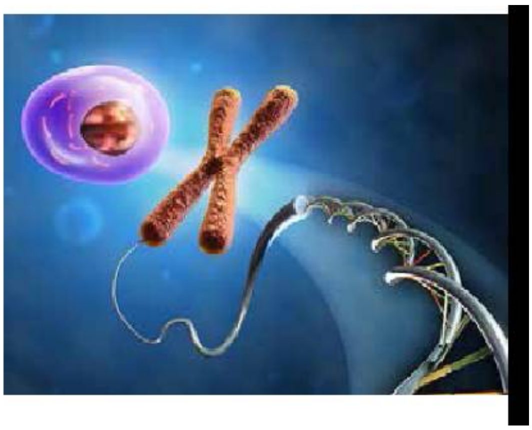
Metaphors for Systems Chemistry

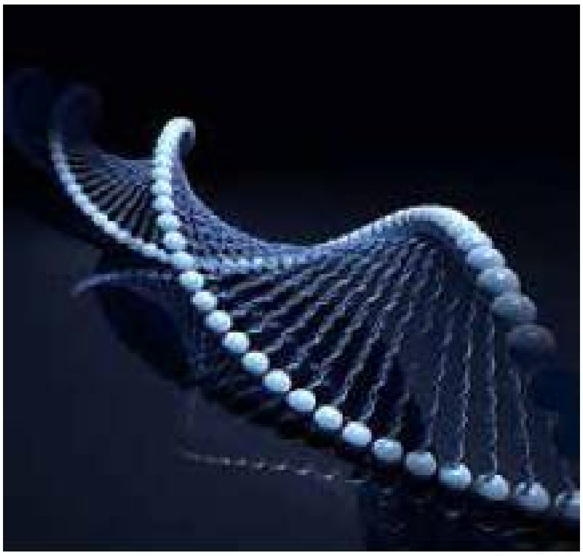
Bioorganic	Mother		Artificial-intelligence Philosophy, cosmology	Second- and third-degree cousins,
Prebiotic	Father		Systems chemistry	Got married to a foreigner
Homochirality	Sister		Supramolecular	Her maiden name

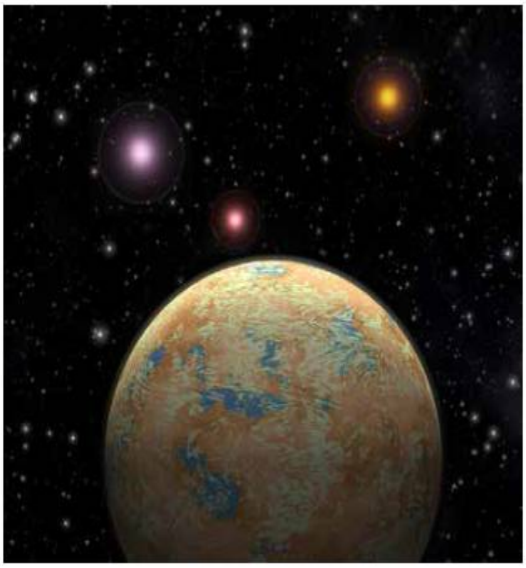
Composomedynamic-kinetic	Twins	Spatiotemporal	Extravagant auntie
Metabolism	Uncle	Nano-tech Single-molecule,	Far-out twins
Compartment	Auntie	Ms. Bz (Belousov–zhabotinsky)	Wet nurse
Evolutionary-genetics	Grandma	If it's a girl her name will be kinetic asymmetry If it's a boy Kay ratchet	Systems chemistry and supramolecular are in expectancy
Synthesis	Only grandpa		

Systems

System	☞ A complex unity ☞ Formed of many diverse modules ☞ Serving a common purpose	
	Examples:	[[Society, Stock Markets] [WWW; web-based social networks] [Echosystems [Climate]] [Economics, Urban Planning, Ecology] [Biology, Physics, Chemistry] [Metabolic Path Ways] [Engineering, Computer Science, Mathematics]]







Complex chemical systems (RNA, DNA, Genes) with Physics/ chemistry/ biology based interactions in start-of-life and its sustainance, propagation, evolution and termination

Complex +
Systems (Energy {material {Life; Non-life}; Non-material}) +
Analysis→
Systems_Analysis

	Chemistry	
Low energy	Green	High energy

	Conventional (or reductionist or as-it-is-in 2020) chemistry
Chemistry	🕮 Focused on the challenges of forming covalent/mechanical bonds 🕮 Determining the structure of chemical molecules/species 🕮 Emphasis on synthesis of pure (natural, exotic) compounds - Requires highly knowledgeable human intervention

Chemists' Practice	✓ Most chemists have been conditioned to study substances in isolation ✓ Reason:For a long time, complex mixtures were intractable

	+ Reagents purified
	+ Experimental control
	  o Temperature, pressure, and humidity
	+ Experimental durations
	  o Shorter than grant cycles
	+ External influences
	  o Avoided minimized
	+ Replication If feasible and reproducible
	+ Precise knowledge
	  o Properties of individual molecules, bulk
	  o one-to-one interactions
	+ Synthetic approaches mixtures of compounds are treated as an unwanted
	feature that must be eliminated

Extant chemists	+ Ability to design and create new molecules
	- Purely chemical approach
	  o not likely to yield life-like modules
	  ! **Remedy**:a holistic approach is key to help unravel such systems and to experimentallyaddress questions related to the chemicalorigins of life

Chemical Evolution	🕮 Chemical element, chemical energy 🕮 Chemical engineering 🕮 Chemical equation, chemical equilibrium, 🕮 Chemical fingerprint, Chemical Mace, chemical machining, chemical name, chemical peel

Biology

Biology is immensely complex at almost every level	☞ Network of atomic interactions → o Conformation or folding of bio-macromolecules (ex: proteins) ☞ Organisation of o Biomolecules into cells o Cells to higher organisms ☞ Network of interactions o Between different organisms and surroundings (ecology)

Biological systems	Plethora of 📖 Complex interconnected signaling systems 📖 Metabolic networks With 📖 Multiple checkpoint controls 📖 Feedback loops → Allowing biological systems to adapt and respond rapidly to external stimuli

Microorganisms to humans

Simplest microorganisms known onEarth	Breathtakingly complex
Complex life systems Human being	Zillion fold complex

Systems biology

Systems biology	☞ Deals with relation between ! Function of a biological system (a cell/specific cellular process) & ! Interactions between various molecular components
	Focuses on deconvoluting complexityfrom already existing superstructures encountered
	☞ In a human cell, some 25,000 genes ☞ Cycles linking spontaneous and non-spontaneous chemical and physicalprocesses ☞ Build rough copies of themselves

Aim	Topredict, repair, control design and realize a biologicalsystem
What is possible today?	Understanding improving at systems level
Tools	o DNA sequencers o Microarray analysis o Mass spectrometry
Trans-disciplines	o Genomics o Proteomics o Metabolomics

Complex Systems Analysis + Biology+ Life→ Systems_Biology

II . Select Research titles (2000 to 2020). ……SytemsChemistry……

	Review
📖 Systems chemistry	
Chem. Soc. Rev. 2017 DOI: 10.1039/c7cs00117g	GonenAshkenasy, Thomas M. Hermans, Sijbren Otto Annette F. Taylor

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
📖 Prebiotic Systems Chemistry: New Perspectives for the Origins of Life	
Chem. Rev. 2014, 114, 285−366 dx.doi.org/10.1021/cr2004844	Kepa Ruiz-Mirazo, Carlos Briones, Andrés de la Escosura

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Chapter
📖 Systems Chemistry Sketches,Chapter 17	
ACS Symposium Series , Vol. 981,Chemical Evolution across Space & Time. Chapter 17, pp 310–324 DOI: 10.1021/bk-2008-0981.ch017.	Stuart A. Kauffman

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
📖 Prebiotic Peptides: Molecular Hubs in the Origin of Life	
Chem. Rev. 2020, 120, 11, 4707–4765 doi.org/10.1021/acs.chemrev.9b00664	Moran Frenkel-Pinter, MousumiSamanta, GonenAshkenasy, Luke J. Leman

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
📖 Systems chemistry	
Chem. Soc. Rev., 2008, 37, 101–108 DOI: 10.1039/b611921m	R. Frederick Ludlow and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 The Beginning of Systems Chemistry	
Life 2019, 9, 11 doi:10.3390/life9010011	Peter Strazewski

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
📖 Achieving biopolymer synergy in systems chemistry	
Chem. Soc. Rev., 2018,47, 5444-5456 DOI: 10.1039/c8cs00174j	Yushi Bai, Agata Chotera, Olga Taran, Chen Liang, GonenAshkenasy and David G. Lynn

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
📖 Dynamic Molecular Networks: From Synthetic Receptors to Self-Replicators	
Acc. Chem. Res. 2012, 45, 12, 2200–2210 doi.org/10.1021/ar200246j	Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
📖 Small-Molecule Systems Chemistry	
Chem 2, 502–524, April 13, 2017	Ognjen S. Miljanic

Reviewed advances in systems-level understanding of
(1) Dynamic combinatorial libraries
(2) Autocatalysis
(3) Oscillatory reactions
(4) Chemical reactivity at origin of life

Nascent efforts in areas that have traditionally not used syst.chem.approach
(5) Reaction discovery
(6) Synthesis & functional utilizationof complex molecules

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
🕮 Prebiotic Systems Chemistry: Complexity Overcoming Clutter	
Chem 2, 470–501, April 13, 2017 doi.org/10.1016/j.chempr.2017.03.001	Saidul Islam and Matthew W. Powner

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Mini Review
🕮 Systems Biology and Systems Chemistry:New Directions for Drug Discovery	
Chemistry & Biology 19, January 27, 2012,23-28	J.B. Brown and Yasushi Okuno

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	eview
🕮 The evolution of metabolism: How to test evolutionary hypotheses at the genomic level	
Computational and Structural Biotechnology JournalVolume 18, 2020, Pages 482-500	Federico ScossaAlisdair R. Fernie

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Review
🕮 Toward Self-Constructing Materials: A Systems Chemistry Approach	
Acc. Chem. Res. 2012, 45, 12, 2178–2188 doi.org/10.1021/ar2002655	Nicolas Giuseppone

	Review
🕮 Chemical Origins of Life: Its Engagement with Society	
Trends in Chemistry, Volume 2, Issue 5, May 2020, 406-409 doi.org/10.1016/j.trechm.2020.02.011	Ramanarayanan Krishnamurthy

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Perspectives
🕮 Toward a general theory of evolution: Extending Darwinian theory to inanimate matter	
Journal of SystemsChemistry 2011 2:1, doi:10.1186/1759-2208-2-1	Addy Pross

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

	Encyclopedia
🕮 Systems Chemistry	
Encyclopedia of Astrobiology DOI 10.1007/978-3-642-27833-4_1095-2	Jan W. Sadownik and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Strategies for Exploring Functions from Dynamic Combinatorial Libraries	
Chem Systems Chem 2020, 2, e2000019 (2 of 11) doi.org/10.1002/syst.20200001	Chunman Jia, Dawei Qi, Yucang Zhang, Kari Rissanen and Jianwei Li

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Recent highlights in systems chemistry	
Current Opinion in Chemical Biology 2009, 13:705–713	Jerome JP Peyralans and Sijbren Otto

🕮 Complex Molecules That Fold Like Proteins Can Emerge Spontaneously	
J. Am. Chem. Soc. 2019, 141, 1685−1689, DOI: 10.1021/jacs.8b11698	Bin Liu, Charalampos G. Pappas, Ennio Zangrando, Nicola Demitri, Piotr J. Chmielewski, and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Systems chemistry: using thermodynamically controlled networks to assess molecular similarity	
Journal of Systems Chemistry 2013 4:2. doi:10.1186/1759-2208-4-2	Vittorio Saggiomo Yana R Hristova R Frederick Ludlow and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 The systems perspective at the cross roads between chemistry and biology	
Journal ofTheoreticalBiology381(2015)11–22 doi.org/10.1016/j.jtbi.2015.04.036	A.delaEscosura, C. Briones, KepaRuiz-Mirazo

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Founder of systems chemistry and foundational theoretical biologist: Tibor Gánti(1933–2009)	
Journal ofTheoreticalBiology381(2015) 2–5 http://dx.doi.org/10.1016/j.jtbi.2015.04.037	EörsSzathmáry

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 EssayThe Essence of Systems Chemistry	
Life 2019, 9, 60 doi:10.3390/life9030060	Peter Strazewski

🕮 From chemical systems to systems chemistry: Patterns in space and time

CHAOS 25, 097613 (2015)	Kenneth Showalter and Irving R. Epstein

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Emergence of a New Self-Replicator from a Dynamic Combinatorial Library Requires a Specific Pre-Existing Replicator

J. Am. Chem. Soc. 2017, 139, 13612−13615 DOI: 10.1021/jacs.7b07346	Yigit Altay, MenizTezcan and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Welcome Home, Systems Chemists! Editorial

Journal of Systems Chemistry 2010, 1:1, 2-6 doi:10.1186/1759-2208-1-1	Günter von Kiedrowski, Sijbren Otto, Piet Herdewijn

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Complexity in Chemistry

Science VOL 284 2 APRIL 1999,89-92	George M. Whitesides and Rustem F. lsmagilov

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Reaction: Thinking-Species Chemistry and the World's Problems

Chem 2, 155–159, February 9, 2017,158-159	Sijbren Otto

Systems chemistry: using thermodynamically controlled networks to assess molecular similarity	
Journal of Systems Chemistry 2013, 4:2 doi:10.1186/1759-2208-4-2	Vittorio Saggiomo Yana R Hristova R Frederick Ludlow and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

Perspective Biology-Inspired Supramolecular Peptide Systems	
Chem 6, 1222–1236, June 11, 2020	Ayala Lampel

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

The Origin and Evolution of Organic Matter in Carbonaceous Chondrites and Links to Their Parent Bodies	
Primitive Meteorites and Asteroids,Book chapter, pages 205-271 DOI: 10.1016/B978-0-12-813325-5.00003-3	Daniel P. Glavin, Conel M.O'D. Alexander, José C. Aponte, Jason P. Dworkin, Jamie E. Elsila, HikaruYabuta,

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

Directed Non-targeted Mass Spectrometry and Chemical Networking for Discovery of Eicosanoids and Related Oxylipins	
Cell Chemical Biology 26, 2019, 433–442 doi.org/10.1016/j.chembiol.2018.11.015	JeramieD.Watrous, T.J. Niiranen, Kim A. Lagerborg, E.A. Dennis, S. Cheng, Mohit Jain

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

Reaction: A Plea for Hypothesis-Driven Research in Prebiotic Systems Chemistry	
Chem 5, 2019, August 8, 1917–1923	Kepa Ruiz-Mirazo

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 Systems biology approaches integrated with artificial intelligence for optimized food focused metabolic engineering

Metabolic Engineering Communications, Vol. 11, December 2020, e00149 doi.org/10.1016/j.mec.2020.e00149	Mohamed Helmy, Derek Smith, Kumar Selvarajoo

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 The nature and mathematical basis for materialstability in the chemical and biological worlds

Journal of Systems Chemistry 2014, 5:3 doi:10.1186/1759-2208-5-3	Robert Pascal and Addy Pross

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 On the divide between animate and inanimate

Journal of Systems Chemistry (2015) 6:2, 1-3 DOI 10.1186/s13322-015-0008-8	ArtoAnnila and ErkkiKolehmainen

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

Life

📖 Understanding the Origins of Life - the Constituents of InterstellarMedium as the Source of Life's Building Blocks

Biophysical Journal 118(3):339a-340a DOI: 10.1016/j.bpj.2019.11.1891	Anita Ra´gyanszki, Hongchen Ji, Rene Fournier

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 100th Anniversary of Macromolecular Science Viewpoint: TowardArtificial Life-Supporting Macromolecules

ACS Macro Lett. 2020, 9, 185−189 doi.org/10.1021/acsmacrolett.9b00938	Jean-François Lutz

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Reaction:Life Is Messy

Chem 5, August 8, 2019,1917–1923 doi.org/10.1016/j.chempr.2019.05.004	Irving R. Epstein

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Introduction—Panspermia,2020;106:1-4

Advances in Genetics, 2020 doi.org/10.1016/bs.adgen.2020.04.001	Edward J. Steele

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Estimating Equilibrium Constants for Aggregation from the Product Distributionof a Dynamic Combinatorial Library

Organic Letters 2009, Vol. 11, No. 22, 5110-5113	Rosemary A. R. Hunt, R. Frederick Ludlow and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Synthesis of the First Triphosphabutadiene"

Chem. Inf. Ed. Engl. 25 (1986) No. 10, 932-935	By Rolf Appel, Barbel Niemann, Winfried Schuhn, andFalk KnochAngew.

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

🕮 Systems Chemistry: Kinetic and Computational Analysis of a Nearly Exponential OrganicReplicator

Chem. Int. Ed. 2005, 44, 6750 –6755 DOI: 10.1002/anie.200501527	MaikKindermann, Insa Stahl, Malte Reimold, Wolf Matthias Pankau, and Gnter von Kiedrowski Angew.

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 New concept for quantification of similarity relates entropy and energy of objects: First and Second Law entangled, group behavior of microblack holes expected

Journal of Systems Chemistry 2010, 1:2, 2-10

Petr Zimak, Silvia Terenzi, Peter Strazewski

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 Spontaneous Emergence of Self-Replicating Molecules Containing Nucleobases and Amino Acids

Strategies using DCA for fabrication of *chimeric* amino acid/nucleobase

- Mixing nucleobase- and peptide-based building blocks→ ligation of these two gives rise to →highly specific chimeric ring structures
- Starts from peptide nucleic acid building blocks

- Earlier report: Nucleic acid-based self-replicating systems
  - Relies on pre-synthesis of (short) oligonucleotide sequences
  - Self-assembly, spontaneously giving rise to an ordered one-dimensional arrangement of nucleobase nanostructures

Self-replication

J. Am. Chem. Soc. 2020, 142, 184−4192
doi.org/10.1021/jacs.9b10796

Bin Liu, Charalampos G. Pappas, Jim Ottelé, Gaël Schaeffer, Christoph Jurissek, Priscilla F. Pieters, Meniz Altay, Ivana Marić, Marc C. A. Stuart, and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 The Lipid world

Origins of Life and Evolution of the Biosphere 31: 119–145, 2001

Daniel Segré, Dafna Ben-Eli, David W. Deamer And Doron Lancet

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 A speculative review of factors controlling the evolutionof phytoplankton during Paleozoic time

Journal of Micropaleontology, 51 (2008) 9–21doi:10.1016/j.revmic.2007.01.007

Paul K. Strother

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 Solvent Composition Dictates Emergence in Dynamic Molecular Networks Containing Competing Replicators

J. Am. Chem. Soc. 2015, 137, 5, 2067–2072 DOI: 10.1021/ja512644f	Giulia Leonetti and Sijbren Otto

Systems Chemistry — [Complex Chemistry]/ Systems — Non-Bonding — Physics — Biology — Photons — Phonons — Electromagnetic — Electrical — Quantum — gravity

📖 Is the transition from chemistry to biology amystery?

Journal of Systems Chemistry 2010, 1:3	Hans Kuhn

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📖 Suitable energetic conditions for dynamic chemical complexity and the living state

Journal of Systems Chemistry 2012, 3:3	Robert Pascal

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📖 Catalyst: Can Systems Chemistry Unravel the Mysteries of the Chemical Origins of Life?

Chem 5, 1917–1923, August 8, 2019	Daniela Kroiss, GonenAshkenasy, Adam B. Braunschweig, Tell Tuttle, and Rein V. Ulijn

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Information Source	ACS.org ; sciencedirect.com
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