ISSN 2724-6132 / 2021-5



# Reports of the workshops:

Scoping workshop on Stem Materials - Rome 2017 Stem Materials: Clues and Path Identification - Rome 2018 Step Towards Stem Materials - Brussels 2019

# WG MATERIALS

Science and Technology Foresight: from society to research National Research Council of Italy



National Research Council of Italy







Schematic view of the concept of Stem Materials: understanding the functioning of living organisms and their interaction within the ecosystem (here represented in yellow as the marine gastropod mollusk named "pelican's foot") is approached through the integration of different aspects (in hexagons) which allows to identify building blocks (in red) to be assembled for a new generation of intelligent materials.

> **Editors:** Pier Francesco Moretti, Ruggero Casacchia

**Copy editing and graphycs** Pier Francesco Moretti, Francesco Verginelli

**Publisher** @2021, Consiglio Nazionale delle Ricerche

All rights reserved

ISSN 2724-6132 / 2021-5





# Preface

This book describes a three-year brainstorming and results within the Working Group Materials of the CNR-S&T Foresight project (<u>http://www.foresight.cnr.it/working-groups/wg-materials.html</u>), from 2017 to 2019.

Three workshops have been organized to debate and identify the path towards the realization of Stem Materials, whose concept will be addressed in details in the next pages.

Scientists from different disciplines and countries were asked to identify the scientific gaps, priorities and research lines of activities.

A first scoping workshop was held in Rome in March 2017, another Face-to-Face workshop in Rome in December 2018, and the last in Brussels in June 2019.

The rationale, background documents, participants, programme and outputs of the workshops are reported.

A paper entitled "STEM materials: a new frontier for an intelligent sustainable world" has been published in the Springer Nature journal BMC Materials, which summarizes the concepts and the outputs (https://bmcmaterials.biomedcentral.com/articles/10.1186/s42833-019-0004-4).





# Steps towards Stem Materials<sup>1</sup>

## The concept of Stem Materials

In nature, living organisms consist of a limited number of primary components and chemical bonds organized in complex systems capable to adapt to diversified environmental conditions. Materials are very rarely adaptable, and often require a large number of components to achieve high performances in specific functions. In this comparison between organisms and materials, the approach to their respective life-cycles are also largely different, the former renewing in a continuous interaction with the environment, the latter mainly preserving from alterations.

Indeed, materials able to perform different functions and to respond to external inputs will become increasingly important. They will play a fundamental role in the additive production to the extent that these are designed and structured to perform specific operations and selfadapt to varying external conditions, without any additional device. This generation of materials can substitute robots in some applications, i.e. when communication and electronics are considered vulnerable aspects.

Materials able to perform as sensors and actuators, accordingly to external environmental conditions for fulfilling different requirements, are still a challenge. These intelligent materials should be flexible in any context and condition, and possibly consist of *primitive units*, containing the minimal and sufficient number of components to perform a basic function, whose *combinations* can respond to specific requests of *multi-functionality and adaptability*.

The required approach is well-known in science, looking for a bridge between the observable macroscopic and the microscopic levels, towards a coherence between descriptions of reality and complexity. It is not simply a matter of promoting inter and cross-disciplinarity, but in understanding the relationships between fundamental scientific theories and contingent conditions or environments, which can play a role in the emergence of new features.

### The process to identify scientific and technological gaps

In **March 2017**, the CNR-S&T Foresight Group on Materials and some (approximately ten) Italian scientists met to exchange views and feasibility of the concept of "Stem Materials". It was recognized that we are facing unprecedented impacts from simulations and processing in material sciences as well as from chemical synthetic biology, where their common approach is by trials or mimicking nature.

During that "scoping" workshop, they identified the main aspects considered relevant for investigation in order to proceed:

<sup>\*</sup> The adjective "stem", commonly attributed to cells, refers to the use of blocks of primitive and nonspecialized materials which, even if not able to differentiate spontaneously in several other types, undergo a process of transformation aimed to make them capable to adapt to specific requirements.





A) non-equilibrium, B) context dependency, C) multiscale, D) cognition, E) assembling, F) synthetic biology, G) sustainability. These aspects ask for advances in physics, computational sciences, biology, chemistry. The "sustainability" carries a dual meaning: from the point of view of materials, the link with elements/critical raw materials and the end of cycle, from the point of view of biology, the concepts of homeostasis and autopoiesis.

The main dilemma remains in paving the way and adopting action towards a general and breakthrough framework for primitive units, as a sort of ribosome of Materials and their combinations, which can enable the multi-functionality and adaptability of materials.

Based on those inputs, approximately twenty international experts accepted the invitation to join a Face-to-Face (F2F) workshop, where they were asked to discuss in detail some specific characteristic to focus on. A background document has been prepared and distributed to frame the concept and support the briefing of the participants, who were contacted one by one by phone or via email.

The F2F workshops are invitation only events, organized in such a way as to guarantee to participants from a range of backgrounds and positions the conditions necessary for a free and open debate. This approach is designed to facilitate convergence towards common positions related to research priorities, knowledge gaps and funding needs..

This F2F workshop was articulated in three days in **December 2018**: during the first one, five experts were invited to introduce all the other participants to different issues which could be useful and probably not known by the whole community: The Materials' Genetic code, Living Materials, Non equilibrium of nanostructures, The role of chaos and rhythms in order and functioning, A whole-cell computational model: phenotype from genotype.

These five talks warmed-up the multi-disciplinary debate.

The second day, a first round of parallel sessions was conducted, where the composition of experts of one session was mainly composed by materials scientists. In this round, bottom-up reflections were collected and reported in the successive plenary session. A second round of parallel sessions, with mixed compositions, were guided to focus on common aspects and proposals. The outputs were reported in the last plenary session of the second day and then analyzed during the last day.

A preliminary discussion on the complexity of Stem Materials suggested to think about them as material systems/machinery. In addition, when addressing the issue of functionality, the main principles has to be specified to identify what properties these materials should show.





## The Identification of clues and path

The experts attending the F2F workshop in December 2018 first identified some characteristics/aspects which are considered interesting, or challenging, and which can provide clues for a new generation of materials.

In the following, these aspects are described.

a) Structure and spatial configuration is crucial for the properties and therefore for function.

b) Thresholds, interfaces, gradients, quorum sensing are all aspects linked to the relevance of non linear behavior and non-equilibrium status which characterize the adaptability and "intelligence" of Stem materials.

c) temporal fluctuations, waves and phase locking can play a fundamental role in ordering and triggering self-organization of the structures.

d) Self-replication is still an enigma to reproduce.

That said, two keywords were extracted to summarize the first round of reflections:

## dynamics of processing + interfaces.

Further exchanges of view between the experts converged on some key aspects to focus the attention in running researches or future developments, as:

the **transport/meaning of info/energy**, that is the communication flow inside the system and its language/code;

the role of **networks and scales** present in the structure and in the energy/information flow; the structure and role of interfaces and gradients, as well as the presence of non-linear elements;

the **space-time organization/dynamics** and their optimization towards the properties;

the capability to manage **multi-states systems**, which are not local in time and are dependent on the history of the process.

These aspects have been already addressed in recent studies on self-organizations of complex systems, in particular in addressing collective dynamics in small worlds networks or in local and global self-entrainments, but the emerging of scaling in networks as well as the role of design has still to be understood (see references to the Rome workshop).

The experts translated their reflections into a concrete proposal which can provide breakthrough clues towards Stem Materials, and in general to any system which can be considered dynamically sustainable.

They proposed to **identify a case study** to address the simplest "logic scheme" which transform a state A in B, then in C and coming to A again (see figure 2, named for sake of simplicity **ABCA** scheme, and as the AbraCAdabra experiment!).

The states A,B,C can represent functions of the same material system or chemical compounds or whatever transformation in a closed loop.

The AbraCAdabra could be meant as a sort of **digi-twin**, in the sense of validating models and theory accordingly to an experimental set-up and trials to be run.

### Towards an operational plan: experiments vs theoretical models

The challenges and aspects referred as relevant in the previous workshops have been already addressed in many studies on self-organizations of complex systems, in particular in





addressing collective dynamics in small worlds networks or in local and global self entrainments. In this context, the role of design has still to be understood and translated into real examples.

A workshop, held in Brussels in **June 2019**, was co-organized in cooperation with the Universitè Libre de Bruxelles, to identify some state-of-the art models which can be considered appropriate to be applied for stem materials.

**Non-equibrium systems and dynamical ordering** were at the core of the debate. Different model classes were also shown: **oscillatory/autocalytic feedback, two-step aggregation, hierarchical models**.

A proposal for the ABCA study has also been presented and the possibility to include the support of digital-twins tools has been discussed.

Finally, some experimental "dilemmas" were reported as food for thoughts, involving experienced and young researchers too.

The main outputs can be summarized as follows:

1) the awareness that mimicking nature is not the best solution, but **understanding the biological systems and multi-disciplinarity** are fundamental to proceed towards stem materials;

2) many **models are available and seem promising**: they have to be adapted to concrete examples in order to understand what theories are the appropriate to reproduce the reality;

3) the role of energy and information flows are crucial and can be treated, but indeed the **synchronism** between different variables is still difficult to be described and interpreted;

4) a **simplification in the communication** of the main principles and aspects of theory is needed: to facilitate the mutual dialogue with experimentalists and allow the use of tools in supporting visualization and clustering of concepts;

4) at least one ABCA case study has been identified.



The way towards Stem Materials: experts in 2018 converged on some key aspects to focus the attention in running researches or future developments.



#### List of annexes

- National Research Council of Italy
- 1. Programme of the workshop in Rome March 2017
- 2. Programme of the workshop in Rome December 2018
- 3. Programme of the workshop in Brussels June 2019
- 4. List of participants to the workshops
- 5. References for the workshops
- 6. Background document and references
- 7. Pics of the workshops





# Annex 1 Scoping Workshop on "Stem Materials"

23-24 March 2017

Aula Volterra – CNR Headquarters - P.le a. Moro 7, Rome, Italy

23 March - 14:00 - 18:30

14:00 – 14:15 Welcome (Massimo Inguscio)

Session I: Introduction and Presentation of participants

Moderator: Giorgio Einaudi

14:15 – 14:30 The Foresight project and scope of the workshop (Ezio Andreta)

14:30 – 16:30 Presentations (10 minutes each) by the participants on their experience and possible contribution to the foresight exercise.

16:30 – 16:45 Coffee break

Session II: Joint brainstorming

Moderator: Pier Francesco Moretti

Rapporteur: Vincenzo Maiorano

16:45 - 17:00 Challenges/open issues towards Stem Materials (Pier Francesco Moretti) 17:00 - 18:30 Open discussion guided by the background document

20:00 Dinner

24 March – 9:00 – 13:00

Session III: Needs and gaps

Moderator: Giorgio Einaudi

09:00 – 09:15 Messages to be detailed (Vincenzo Maiorano)

09:15 – 11:15 Open discussion and additional questions

11:15 – 11:30 Coffee break

Session IV: Next steps

11:30 – 11:45 Wrap-up (Pier Francesco Moretti and Vincenzo Maiorano)

11:45 - 12:00 Next steps: face-to-face international workshop et al. (Giorgio Einaudi)

12:00 - 12:45 Open discussion

12:45 - 13:00 Closing remarks (Ezio Andreta)

13:00 - 14:00 Light Lunch

SIDE EVENT "Materials for Energy"

Session V: Possible synergies between the Foresight on Materials and Energy Moderator: Antonino Salvatore Aricò

14:30 - 14:45 The outcomes from the scoping workshop on Materials

14:45 - 15:00 The Working Group on Energy: the proposal and its updates

- 15:00 15:15 Possible synergies between the two groups: focus on Energy Storage, Management and Valorization of CO2
- 15:15 16:30 Open discussion

16:30 - 17:00 Wrap-up and next steps





### Annex 2

# Face-to-Face Workshop on "Stem Materials"

## 12-14 December 2018

Sheraton, Parco de' Medici Rome Hotel, Viale Salvatore Rebecchini 145, Rome, Italy

12 December – Warm-up (14:30 – 18:00)

- 13:00 14:30 Light Lunch
- 14:30 14:45 Welcome (Massimo Inguscio President of CNR, TBC)
- 14:45 15:00 The back casting foresight approach (Ezio Andreta)
  - Setting the Scene (Pier Francesco Moretti)
- 15:00 16:00 Introduction to
  - The Materials' Genetic code (Nicola Marzari) + Q&A
  - Living Materials systems (Olga Speck) + Q&A
- 16:00 16:30 Coffee break
- 16:30 18:00 Introduction to
  - Non-equilibrium of nanostructures (Bartosz Grzybowski) + Q&A
  - The role of chaos and rhythms in order and functioning (Vasileios Basios) + Q&A
  - A whole-cell computational model: phenotype from genotype (Maria Suarez Diez) + Q&A
- 18:00 18:15 Rules for the day after: composition of two groups.
- 20:00 Dinner

13 December – Brain storming

- 09:00 11:00 Parallel sessions: open and guided discussion
- 11:00 11:30 Coffee break
- 11:30 13:00 Plenary: Report from parallel sessions and reflections
- 13:00 14:00 Light Lunch
- 14:00 16:00 Parallel sessions: open and guided discussion
- 16:00 16:30 Coffee break
- 16:30 18:00 Plenary: Report from parallel sessions and reflections
- 20:00 Dinner

#### 14 December – Suggestions

- 09:00 10:30 Points of view: commonalities and diversities
- 10:30 11:00 Coffee break
- 11:00 13:00 Suggestions towards next steps
- 13:00 14:00 Light Lunch





## Annex 3

# Workshop Steps towards "Stem Materials"

25-26 June 2019 Solvay Room – Universitè Libre de Bruxelles – Campus de la Plaine, N.O. Bldg, Brussels Organized in the framework of the Science and Technology Foresight Project of the National Research Council of Italy (http://www.foresight.cnr.it/materials)

25 June - 14:00 - 18:00

## Session I: Visions vs gaps

Chair: Dr. Vasileios Basios

14:00 – 14:10 Welcome: "Nonequilibrium systems: an inspiration & source of innovation" (Prof. Mustapha Tlidi, President of the Physics Dept., ULB)

14:10 – 14:40 "Active colloidal particles: nonequilibrium dynamics and self-organization" (Prof. Pierre Gaspard, Head of Physics of Complex Systems, Dept., ULB)

14:40 – 15:10 "The challenges of new generations of materials"

(Prof. Rodrigo Martins - UNINOVA/CEMOP)

15:10 – 15:40 "The inspiration from nature" (Prof. Olga Speck - FIT Uni Freiburg)

15:40 – 16:10 "The foresight on Stem Materials" (Dr. Pier Francesco Moretti - CNR)

16:10 – 16:30 Coffee break

Session II: Feasibility

Chair: Prof. Rodrigo Martins

16:30 – 17:00 "European vision and opportunities" (Dr. Barend Verachtert – EC DG RTD) 17:00 – 18:00 Discussion

26 June - 9:00 - 15:00

Session III: A path towards a new generation of materials

Chair: Dr. Pier Francesco Moretti

09:00 – 09:15 "The Foresight on Stem materials: sprouting from Rome to Brussels"

09:15 – 09:45 "A possible idea for 'ABCA' "(Dr. Luigi Ambrosio - CNR)

09:45 – 10:25 "Possible model classes" (Dr. Vasileios Basios - ULB)

10:25 – 10:50 Coffee break

Session II: Brainstorming

Chair: Prof. Olga Speck

10:50 – 11:30 "Self-organized precipitation reactions in non-equilibrium conditions" (Dimitra Spanoudaki, Fabian Brau, Anne De Wit - ULB)

- 11:30 12:00 "The role of vesicles" (Dr. Gianfranco Peluso CNR)
- 12:00 13:00 Discussion: The big questions on and for STEM materials

13:00 – 13:45 Light Lunch

13:45 - 15:30 Discussion: Outlook for the (near) future





Annex 4 List of participants to the workshops

		-		
Name	Affiliation	Workshop 2017	Workshop 2018	Workshop 2019
Tommaso	Iuelich			
	·	1	1	
		1		
-			1	1
	CNR	1	1	
Cecilia	CNR		1	
Vasileios	ULB		1	1
Ruggero	CNR	1	1	
	CNR		1	
Paolo	ISS/INFN		1	
Giorgio	CNR	1	1	1
Alberto				
Paolo				
				1
				_
		1		
				1
		1		
			1	
				1
0	EPFL	1	1	
	CNR	1		
Pier	CNR	1	1	1
Francesco				
Maria Grazia	CNR		1	1
	Politecnico Torino	1	1	
				1
-		1		
	*			1
				1
				1
				1
_				1
				1
· · · · · · · · · · · · · · · · · · ·	European Commission			1
	Vasileios Ruggero Caterina Paolo Giorgio Alberto Paolo Elvira Bartosz Michele Natalie Liberato Vincenzo Rodrigo Nicola Alessandro Pier Francesco	NameAffiliationTommasoJuelichAndreaCNRPier LuigiSwiss Fed. Inst. of Technology in ZurichLuigiCNREzioCNRAntoninoCNRCeciliaCNRVasileiosULBRuggeroCNRCaterinaCNRPaoloISS/INFNGiorgioCNRAlbertoPolitecnico TorinoPaoloPolitecnico TorinoBartoszUlsan Nat. Inst. of Science and Tech.MicheleUniversita' del Piemonte OrientaleNatalieBelgian Nuclear Research CenterLiberatoIstituto Italiano di TecnologiaVincenzoCNRRodrigoUNINOVA/CEMOPNicolaEPFLAlessandroCNRFrancescoMariaGuidoPolitecnico TorinoMariaCNRFrancescoCNRFrancescoCNRGraziaCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianfrancoCNRGianf	2017TommasoJuelich1AndreaCNR1Pier LuigiSwiss Fed. Inst. of Technology in Zurich1LuigiCNR1EzioCNR1CeciliaCNR1CeciliaCNR1VasileiosULB1RuggeroCNR1CaterinaCNR1CaterinaCNR1GiorgioCNR1AlbertoPolitecnico Torino1PaoloISS/INFN1GiorgioCNR1AlbertoPolitecnico Torino1PaoloPolitecnico Torino1BartoszUlsan Nat. Inst. of Science and Tech.1MicheleUniversita' del Piemonte Orientale1NatalieBelgian Nuclear Research Center1LiberatoIstituto Italiano di Tecnologia1VincenzoCNR1RodrigoUNINOVA/CEMOP1NicolaEPFL1AlessandroCNR1Francesco11MariaWageningen University1OlgaFIT Uni Freiburg1Francesco21GianfrancoCNR1GianfrancoCNR1GianfrancoCNR1GianfrancoCNR1GianfrancoCNR1GianfrancoCNR1GianfrancoCNR1GianfrancoCNR1 <tr< td=""><td>NameAffiliationWorkshop 2017Workshop 2018TommasoJuelich11AndreaCNR11Pier LuigiSwiss Fed. Inst. of Technology in Zurich11LuigiCNR11EzioCNR11AntoninoCNR11CeciliaCNR11VasileiosULB11RuggeroCNR11CaterinaCNR11GorgioCNR11GiorgioCNR11AlbertoPolitecnico Torino11PaoloPolitecnico Torino11BartoszUlsan Nat. Inst. of Science and Tech.11MicheleUniversita' del Piemonte Orientale11NatalieBelgian Nuclear Research Center11LiberatoIstituto Italiano di Tecnologia11VincenzoCNR111NicolaEPFL111NicolaEPFL111PierCNR111GiadiónPolitecnico Torino111NicolaEPFL111RodrigoUNINOVA/CEMOP111NicolaEPFL111OlidoPolitecnico Torino111GianfrancoCNR111Guido</td></tr<>	NameAffiliationWorkshop 2017Workshop 2018TommasoJuelich11AndreaCNR11Pier LuigiSwiss Fed. Inst. of Technology in Zurich11LuigiCNR11EzioCNR11AntoninoCNR11CeciliaCNR11VasileiosULB11RuggeroCNR11CaterinaCNR11GorgioCNR11GiorgioCNR11AlbertoPolitecnico Torino11PaoloPolitecnico Torino11BartoszUlsan Nat. Inst. of Science and Tech.11MicheleUniversita' del Piemonte Orientale11NatalieBelgian Nuclear Research Center11LiberatoIstituto Italiano di Tecnologia11VincenzoCNR111NicolaEPFL111NicolaEPFL111PierCNR111GiadiónPolitecnico Torino111NicolaEPFL111RodrigoUNINOVA/CEMOP111NicolaEPFL111OlidoPolitecnico Torino111GianfrancoCNR111Guido





## **References for the workshop in Rome 2018**

- A.L. Barabasi, R. Albert, Emerging of scaling in random networks, 1999, Science, 286, 509-512, and Statistical mechanics of complex networks, 2000, Rev. of Modern Physics, 74, 47-97

- M. Newmann, Applied mathematics: the power of design, 2000, Nature, 405, 412-413

- H. Sakaguchi, S. Shinomoto, Y. Kuramoto, Local and global self-entrainments in oscillator lattices, 1987, Progress in theor Physics, 77, 1005,1010

- K.Y. Tsang, R.E. Mirollo, S.H. Strogatz, K. Wiesenfeld Dynamics of a globally coupled oscillator array, 1991, Physica D, 48, 102-1

- D.J Watts, S.H. Strogatz, Collectve dynamics of small worlds networks, 1998, Nature, 393, 440-442

- K. Wiesenfeld, P. Colet, S.H. Strogatz, Frequency locking in Josephson array: connection with the Kuramoto model, 1998, Phys Rev E, 57, 1563-1569

### **References for the workshop in Brussels 2019**

- Bochynek T, Robson SKA (2014), "Physical and Biological Determinants of Collective Behavioural Dynamics in Complex Systems", PLoS ONE 9(4): e95112

- Gaspard P. & Kapral R. (2019) Thermodynamics and statistical mechanics of chemically powered synthetic nanomotors, Advvances in Physics: X, 4, 1

- Gaspard P. (2016) Kinetics and thermodynamics of living copolymerization processes, Phil. Trans. R. Soc. A, 374

- Gaspard P. (2013) Self-Organization at the Nanoscale Scale in Far-From-Equilibrium Surface Reactions and Copolymerizations, A. S. Mikhailov and G. Ertl, Eds., Engineering of Chemical Complexity, World Scientific, Singapore, ISBN 978-981-4390-45-3, 51-77

- Matsuda H., Ogita N., , Sasaki A., and Sato K. (1992) Statistical Mechanics of Population the lattice Lotka-volterra model, Progress of Theoretical Physics, 88, 6

- Nicolis G & Nicolis C (2005), Kinetics of phase transitions in the presence of an intermediate metastable state: A generic model, Physica A: Statistical Mechanics and its Applications 351(1):22-39

- Nicolis G. (1995) "Introduction to Nonlinear Science", Cambridge Univ. Press

- Nicolis G.& Prigogine I (1977) Self-Organization in Nonequilibrium Systems: From Dissipative Structures to Order through Fluctuations, Wiley, New York





# Annex 6 BACKGROUND DOCUMENT and references CNR S&T Foresight on Stem Materials<sup>2</sup>

## MISSION

In nature, living organisms consist of a limited number of primary components and chemical bonds organized in complex systems capable to adapt to diversified environmental conditions. Materials are very rarely adaptable, and often require a large number of components to achieve high performances in specific functions. In this comparison between organisms and materials, the approach to their respective life-cycles are also largely different, the former renewing in a continuous interaction with the environment, the latter mainly preserving from alterations.

Indeed, materials able to perform different functions and to respond to external inputs will become increasingly important. They will play a fundamental role in the additive production to the extent that these are designed and structured to perform specific operations and self-adapt to varying external conditions, without any additional device. Materials able to perform as sensors and actuators, accordingly to external environmental conditions for fulfilling different requirements, are still a challenge. These intelligent materials should be flexible in any context and condition, and possibly consist of *primitive units*, containing the minimal and sufficient number of components to perform a basic function, whose *combinations* can respond to specific requests of *multi-functionality and adaptability*.

The required approach is well-known in science, looking for a bridge between the observable macroscopic and the microscopic levels, towards a coherence between descriptions of reality and complexity. It is not simply a matter of promoting inter and cross-disciplinarity, but in understanding the relationships between fundamental scientific theories and contingent conditions or environments, which can play a role in the emergence of new features.

### MAIN CHALLENGES

In march 2017, the CNR-S&T Foresight Group on Materials and scientists from different disciplines met to identify the main challenges in addressing the concept of "Stem Materials".

A new paradigm in the modeling of artifacts has already emerged with the digitization of manufacturing, now fueled by advances in additive manufacturing and material science [1].

Several researchers have proposed theoretical foundations and practical implementations of some structures [2,3] that extend the representational capabilities of solid modeling: these

<sup>\*</sup> The adjective "stem", commonly attributed to cells, refers to the use of blocks of primitive and non-specialized materials which, even if not able to differentiate spontaneously in several other types, undergo a process of transformation aimed to make them capable to adapt to specific requirements.





challenges require the capabilities of modeling embedded nano and microstructures, internal geometry architectures, multi-scale behaviors, and composite multi-material objects. In this context, the functional specification of artifact's behavior is the least understood: many abstractions of function and behavior have been proposed [4, 5, 6], but the formal semantics of such models remains unclear [1]. One of the main challenges to break this impasse is to venture beyond static structures into dynamic nanomaterials that organize and/or function out of the thermodynamic equilibrium. In particular, over the last two decades, the focus of materials chemistry and nanotechnology has been gradually shifting from the synthesis of to the synthesis/assembly of hybrid individual nanomaterial organic-inorganic bio-inspired supramolecular aggregates, following three different heterostructure and thermodynamic approaches: "equilibrium", "kinetically trapped" and "far-from-equilibrium" assemblies [7,8]. Heterointegration of materials with different characteristics, including different scales (atomic, nano, meso, macro), chemical character (organic/inorganic), dimensionalities (e.g. interfacing 0D, 1D, and 2D objects altogether), and geometry (e.g. topology), offers a number of still unexplored routes in this respect. For instance, the synthesis/assembly of larger nanostructures and materials has been successful in a variety of structures (molecule-like nanoclusters [9,10,11] 2D nanoparticle arrays [12,13,14] and 3D crystals [15,16] DNA origami [17,18] mesoporous materials [19,20,21]). Although these materials are being used to address important challenges in different applications (catalysis [22], energy conversion [23,24,25], information storage and processing [26], sensing [27,28,29], diagnostics [30,31,32] and therapeutics [33]), a radical progress seems not to be introduced [8].

Materials scientists have explored geneticists' lessons to identify a '<u>materials genome</u>' that encodes the properties of various compounds in the same way that biological information is encoded in DNA base pairs and the way they are arranged in space. In 2003, it was first showed [34] how a database of quantum-mechanics calculations could help to predict the most likely crystal structure of a metal alloy — a key step for anyone in the business of inventing new materials. The design of <u>machine-learning</u> algorithms capable to extract patterns from a library of compounds has provided unprecedented results [35], but even in the case of functional materials, current computer codes work well only for a limited number of cases [36].

Life-like properties of materials, such as multi-functionality, adaptability, re-configurability, taxis [37], internal feedback, or self-replication [38,39] have been definitely proposed to reside outside of thermodynamic equilibrium [40,41,42,43,44,45] and the main challenge is to understand if such "intelligent" materials may provide a range of functions that are not obtained in static, equilibrium materials (e.g., reconfigurable, adaptable, and self-repairing), thereby enabling the emergence of entirely new applications [46].

Understanding how living systems build and operate their nanoscale machinery (molecular recognition, maintenance of non-equilibrium conditions, feedback loop, reaction-diffusion processes, compartmentalization and communication), is foreseen for a successive integration towards functional systems/materials [47].





<u>Chemical synthetic biology</u> (CSB), as the artificial design and engineering of new "quasibiological" materials, , is providing unprecedented outcomes. CSB uses and assembles biological parts, synthetic or not, to create new structures, allowing understanding the roots of biological function and organization [48]. Recently, advances in technologies and reduced costs are enabling a more systematic characterization of natural or artificial products, shedding lights on the potential number of undiscovered structures. This increased capacity suggests that one of the most substantial issues to be investigated is not the discovery of new products but rather the design and the construction of pathways that lead to the desired production [49]. Recent work to build large libraries of genes and regulatory parts have increased the control of gene expression by many orders of magnitude [50,51]. In this context, CRISPR interference has already gained traction in industry, agriculture and medicine as a powerful tool [52,53]. Nevertheless, these results are designed by trial and error, rather than being based on a fundamental understanding of how to build a functioning organism [54].

The identification and design of "primitive units", where minimal and sufficient components are contained to perform a basic function, seems far to come: the concept of a "minimal but complex cell" has been already developed and a "systemic approach" to the whole complex system is required [55,56].

This challenge is addressing the relationships between the components inside the cell and those with the contingent conditions of the external environment. A better understanding of genetic changes enabling living organisms to respond to stress and the definition of the underlying mechanisms of plant adaptation to "unprecedented" environments (such as spaceflight) is already under investigation [57]. Having in mind that most of systems found in nature are not in thermodynamic equilibrium, continuously and discontinuously subject to flux of matter and energy to and from other systems and to chemical reactions, understanding <u>non-equilibrium states</u> is indisputably one of the issues to be addressed [58,59,33].

The issue of non-equilibrium is indirectly linked to an aspect which is asking the material science and biology communities to tackle the challenge of "stem materials": <u>sustainability</u>. If sustainability has been traditionally embedded in the challenge of securing critical raw materials, in living organisms it can be associated to the aspects of homeostasis [60]. In this regard, despite performance is usually opposed to multi-functionality and adaptability, the capability to recycle and convert the environmental resources to address specific needs has to be considered a sort of fil-rouge when designing the next generation of materials.

We would like to thank the participants to the scoping workshop held in Rome on 23-24 March 2017 for their contribution in the elaboration of this document: Tommaso Calarco, Andrea Camposeo, Michele Laus, Pier Luigi Luisi, Liberato Manna, Nicola Marzari, Alessandro Molle, Francesco Stellacci and Angelo Vulpiani.





We are facing unprecedented impacts from simulations and processing in material sciences as well as from chemical synthetic biology, where their common approach is by trials or mimicking nature.

The way forward "Stem Materials", in terms of multi-functionality and adaptability, requires addressing different aspects (see figure 1) which are independently advancing. In this scenario, it is well known that the context fixes the relevant level of description of a reality [61]: fundamental laws do not describe true facts whereas phenomenological laws refer to empirical reality.

The main dilemma is in identifying paths and action towards a general and breakthrough framework for primitive units as a sort of ribosome of Materials and their combinations.



Figure 1: a brief sketch of the aspects identified as those to be addressed for tackling the challenge of stem materials. In blue, those which at the moment seem to be closer to biology, in red those which are mainly framed in physics, material and computing sciences, and in green the aspect of sustainability which addresses both homeostasis and critical raw materials.





#### REFERENCES

1. Regli W., Rossignac J., Shapiro, V., Srinivasan V., 2016, "The new frontiers in computational modeling of material structures", Computer-Aided Design, 77, 73

2. Rossignac J., O'Connor M.A., 1989, "A dimension-independent model for pointsets with internal structures and incomplete boundaries". IBM TJ Watson Research Center

Hoffmann C.M., Rossignac J., 1996, "A road map to solid modeling", IEEE Trans Vis Comput Graphics, 2(1), 3
Gero J.S., Kannengiesser U., 2004, "The situated function-behaviour-structure framework. Des Stud, 25(4), 373

5. Umeda Y., Ishii M., Yoshioka M., Shimomura Y., Tomiyama T., 1996, "Supporting conceptual design based on the functionbehavior-state modeler", Artif Intell Eng Des Anal Manuf, 10(04), 275

6. Sudarsan R., Fenves S.J., Sriram R.D., Wang F., 2005, "A product information modeling framework for product lifecycle management", Comput Aided Des, 37(13), 1399

7. Mattia E., Otto S., 2015, "Supramolecular Systems chemistry", Nat. Nanotechnology, 10, 111

8. Warren S.C., Guney-Altay O., Grzybowski B.A, 2012, "Responsive and Nonequilibrium Nanomaterials", *J. Phys. Chem. Lett.*, 3, 2103

9. Chen S., Ingram R. S., Hostetler M. J., Pietron J. J., Murray R.W., Schaaff T. G., Khoury J.T., Alvarez M. M., Whetten R. L., 1998, "Gold Nanoelectrodes of Varied Size: Transition to Molecule-Like Charging", *Science*, 280, 2098

10. Ragazzon C., Baroncini M., Silvi S., Venturi M., Credi A., 2015, "Light-powered autonomous and directional molecular motion of a dissipative self-assembling system", *Nat. Nanotechnology*, 10, 70

11. Olson M. A., Coskun A., Klajn R., Fang L., Dey S. K., Browne K.P., Grzybowski B. A., Stoddart J. F., 2009, Assembly of Polygonal Nanoparticle Clusters Directed by Reversible Noncovalent Bonding Interactions", *Nano Lett.*, 9, 3185

12. Shevchenko E. V., Talapin, D. V., Kotov, N. A., O'Brien, S., Murray C. B., 2006, "Structural Diversity in Binary Nanoparticle Superlattices", *Nature*, 439, 55

13. Srivastava S., Kotov N. A., 2009, "Nanoparticle Assembly for 1D and 2D Ordered Structures", *Soft Matter*, 5, 1146

14. Murray C. B., Kagan C. R., Bawendi M. G., 2000, "Synthesis and Characterization of Monodisperse Nanocrystals and Close-Packed Nanocrystal Assemblies", *Annu. Rev. Mater. Sci.*, 30, 545

15. Macfarlane R.J., Lee B., Jones M.R., Harris, N., Schatz G.C., Mirkin, C.A., 2011, "Nanoparticle Superlattice Engineering with DNA", *Science*, 334, 204

16. Kalsin A.M., Fialkowski M., Paszewski M., Smoukov S.K., Bishop, K.J.M., Grzybowski B.A., 2006, "Electrostatic Self-Assembly of Binary Nanoparticle Crystals with a Diamond-Like Lattice", *Science*, 312, 420

17. Rothemund P.W.K., 2006, "Folding DNA to Create Nanoscale Shapes and Patterns", *Nature*, 440, 297

18. Andersen E.S., Dong M., Nielsen M.M., Jahn K., Subramani R., Mamdouh W., Golas M.M., Sander B., Stark H., Oliveira C.L.P., 2009, "Self-Assembly of a Nanoscale DNA Box with a Controllable Lid.", *Nature*, 459, 73

19. Yang, P.D., Deng T., Zhao D.Y., Feng P. Y., Pine D., Chmelka B.F., Whitesides G.M., Stucky G. D., 1998, "Hierarchically Ordered Oxides", *Science*, 282, 2244

20. Warren S.C., Messina L.C., Slaughter L.S., Kamperman, M., Zhou, Q., Gruner S.M., DiSalvo F.J., Wiesner, U., 2008, "Ordered Mesoporous Materials from Metal Nanoparticle–Block Copolymer Self-Assembly", *Science*, 320, 1748

21. Klajn R., Bishop K.J.M., Fialkowski M., Paszewski M., Campbell C.J., Gray T.P., Grzybowski B.A., 2007, "Plastic and Moldable Metals by Self-Assembly of Sticky Nanoparticle Aggregates", Science, 316, 261

22. Bell A.T., 2003, "The Impact of Nanoscience on Heterogeneous Catalysis", Science, 299, 1688

23. Gratzel, M. 2001, "Photoelectrochemical Cells", *Nature*, 414, 338

24. Arico A. S., Bruce, P., Scrosati, B., Tarascon, J.M., van Schalkwijk W., 2005, "Nanostructured Materials for Advanced Energy Conversion and Storage Devices", *Nat. Mater.*, 4, 366

25 Wang J., Li Y., Sun X., 2013, "Challenges and opportunities of nanostructured materials for aprotic rechargeable lithium–air batteries", *Nano Energy*, 2, 4, 443

26. Moore G.E., 1998, "Cramming More Components onto Integrated Circuits. Proc. IEEE, 86, 82

27. Elghanian R., Storhoff J.J., Mucic R.C., Letsinger R.L., Mirkin C.,A., 1997, "Selective Colorimetric Detection of Polynucleotides Based on the Distance-Dependent Optical Properties of Gold Nanoparticles", *Science*, 277, 1078

28. Burns A., Sengupta P., Zedayko, T., Baird B., Wiesner U., 2006, "Core/Shell Fluorescent Silica Nanoparticles for Chemical Sensing: Towards Single-Particle Laboratories", *Small*, 2, 723

29. Shipway A.N., Katz E., Willner I., 2000, "Nanoparticle Arrays on Surfaces for Electronic, Optical, and Sensor Applications", *Chem. Phys. Chem.*, 1, 18

30. Han M., Gao X., Su, J.Z., Nie S., 2001, "Quantum-Dot-Tagged Microbeads for Multiplexed Optical Coding of Biomolecules", *Nat. Biotechnol.*, 19, 631

31. Cheng M.M.C., Cuda G., Bunimovich Y.L., Gaspari M., Heath J.R., Hill H.D., Mirkin C.A., Nijdam A.J., Terracciano R., Thundat, T. et al., 2006, "Nanotechnologies for Biomolecular Detection and Medical Diagnostics", *Curr. Opin. Chem. Biol.*, 10, 11

32. Rosi N.L., Mirkin C. A., 2005, "Nanostructures in Biodiagnostics", Chem. Rev., 105, 1547





33. Ferrari M., 2005, "Cancer Nanotechnology: Opportunities and Challenges", Nat. Rev. Cancer, 5, 161

34. Curtarolo S., Morgan D., Persson K., Rodgers J., Ceder G., 2003, "Predicting Crystal Structures with Data Mining of Quantum Calculations", *Phys. Rev. Lett.*, 91, 135503

35. Andreussi O. et al, 2017, "Advanced capabilities for materials modelling with Quantum ESPRESSO", *Journal of Physics: Condensed Matter*, DOI: 10.1088/1361-648X/aa8f79

36. Nosengo N., 2016, "The material code", *Nature*, 533, 25

37. Lagzi I.N., Soh S., Wesson P.J., Browne K.P., Grzybowski B.A., 2010, "Maze Solving by Chemotactic Droplets.", J. Am. Chem. Soc., 132, 1198

38. Patzke V., von Kiedrowski G., 2007, "Self Replicating Systems", ARKIVOC, 293

39. Luther A., Brandsch R., von Kiedrowski G., 1998, "Surface-Promoted Replication and Exponential Amplification of DNA Analogues", *Nature*, 396, 245

40. Rybtchinski, B., 2011, "Adaptive Supramolecular Nanomaterials Based on Strong Noncovalent Interactions", ACS Nano, 5, 6791

41. Mann S., 2009, "Self-Assembly and Transformation of Hybrid Nano-Objects and Nanostructures under Equilibrium and Non-Equilibrium Conditions", *Nat. Mater.*, 8, 781

42. Grzybowski B. A., Stone H.A., Whitesides G.M., 2000, "Dynamic Self-Assembly of Magnetized, Millimetre-Sized Objects Rotating at a Liquid–Air Interface", *Nature*, 405, 1033

43. Whitesides G.M., Grzybowski B.A., 2002, "Self-Assembly at All Scales, Science, 295, 2418.

44. Klajn R., Bishop K.J.M., Grzybowski B.A., 2007, "Light-Controlled Self-Assembly of Reversible and Irreversible Nanoparticle Suprastructures", *Proc. Natl. Acad. Sci.* U.S.A., 104, 10305

45. Fialkowski M., Bishop, K.J.M., Klajn R., Smoukov S.K., Campbell C.J., Grzybowski B.A., 2006, "Principles and Implementations of Dissipative (Dynamic) Self-Assembly", *J. Phys. Chem. B*, 110, 2482

46. Soh S., Byrska M., Kandere-Grzybowska K., Grzybowski B.A., 2010, "Reaction–Diffusion Systems in Intracellular Molecular Transport and Control", *Angew. Chem.*, Int. Ed., 49, 4170

47. Grzybowski B.A., Hack, W.T.S., 2016, "The nanotechnology of life-inspired systems", *Nat. Nanotechnology*, 11, 585

48. Chiarabelli C., Stano P., Luisi P.L, 2013, "Chemical synthetic biology: a mini-review", *Frontiers in microbiology*, 4, 285

49. Smanski M.J., Zhou H., Claesen J., Shen B., Fischbach M.A., Voigt C.A., 2016, "Synthetic biology to access and expand nature's chemical diversity", *Nature Reviews, Microbiology*, 14, 135

50. Mutalik V.K. et al., 2013, "Quantitative estimation of activity and quality for collections of functional genetic elements", *Nature Methods*, 10, 347

51. Chen Y.J., Liu P., Nielsen A.A., Brophy J.A., Clancy K., Peterson T., Voigt C.A., 2013, "Characterization of 582 natural and synthetic terminators and quantification of their design constraints", *Nature Methods*, 10, 659

52. Qi L.S., Larson M.H., Gilbert L.A., Doudna J.A., Weissman J.S., Arkin A.P., Lim W.A., 2013, "Repurposing CRISPR as an RNA-Guided Platform for Sequence-Specific Control of Gene Expression", Cell, 152, 1173

53. Zalatan J.G., Lee M.E., Almeida R., Gilbert L.A., Whitehead E.H., La Russa M., Tsai J.CC., Weissman J.S., Dueber J.E., Qi L.S. , Lim W.A., 2014, "Engineering complex synthetic transcriptional programs with CRISPR RNA scaffolds", Cell, 160, 339

54. Callaway, E. 2016, "'Minimal' cell raises stakes in race to harness synthetic life", Nature, 531, 557

55. Hutchinson, C.A. et al., 2016, "Design and synthesis of a minimal bacterial genome", Science, 351, 6280, aad6253

56. Luisi, P.L., Stano, P., 2011, "Synthetic biology: Minimal cell mimicry", Nature Chemistry, 3, 755

57. Stefano G., Hawes C., Brandizzi F., 2014, "ER - the key to the highway", Curr Opin Plant Biol., 22, 30

58. Demirel, Y., 2010, "Nonequilibrium thermodynamics modeling of coupled biomedical cycles in living cells", Journal of Non-Newtonian fluid mechanics, 165, 953

59. Jona Lasinio, G., 2015, "Understanding non-equilibrium: a challenge for the future", Contributions to Science, 11, 127

60. Meunier, C.L., Malzhan, A.M., Maarten, B., 2014, "A New Approach to Homeostatic Regulation: Towards a Unified View of Physiological and Ecological Concepts", PLOS ONE, 9, e107737

61. Chibbaro S., Rondoni L., Vulpiani A., 2014, "Reductionism, Emergence and Levels of Reality", Springer eds., ISBN 978-3-319-06360-7





## Annex 7

# Pics of the workshop in Rome, March 2017











# Pics of the workshop in Rome, December 2018







# Pics of the workshop in Brussels, June 2019





