Science & Technology FORESIGHT
from society to research

Background Document

"Scoping Workshop on Stem Material"

23-24 March, 2017 - Rome

WG MATERIALS

National Research Council of Italy

BACKGROUND DOCUMENT
CNR S&T Foresight on Stem Materials[1]

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].

---

* 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.

Several researchers have proposed theoretical foundations and practical implementations of some structures [2,3] that extend the representational capabilities of solid modeling: these 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 individual nanomaterial to the synthesis/assembly of hybrid organic-inorganic heterostructure and bio-inspired supramolecular aggregates, following three different 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 'materials genome' 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 machine-learning 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].

Chemical synthetic biology (CSB), as the artificial design and engineering of new "quasi-biological" 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 non-equilibrium states 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": sustainability. 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.

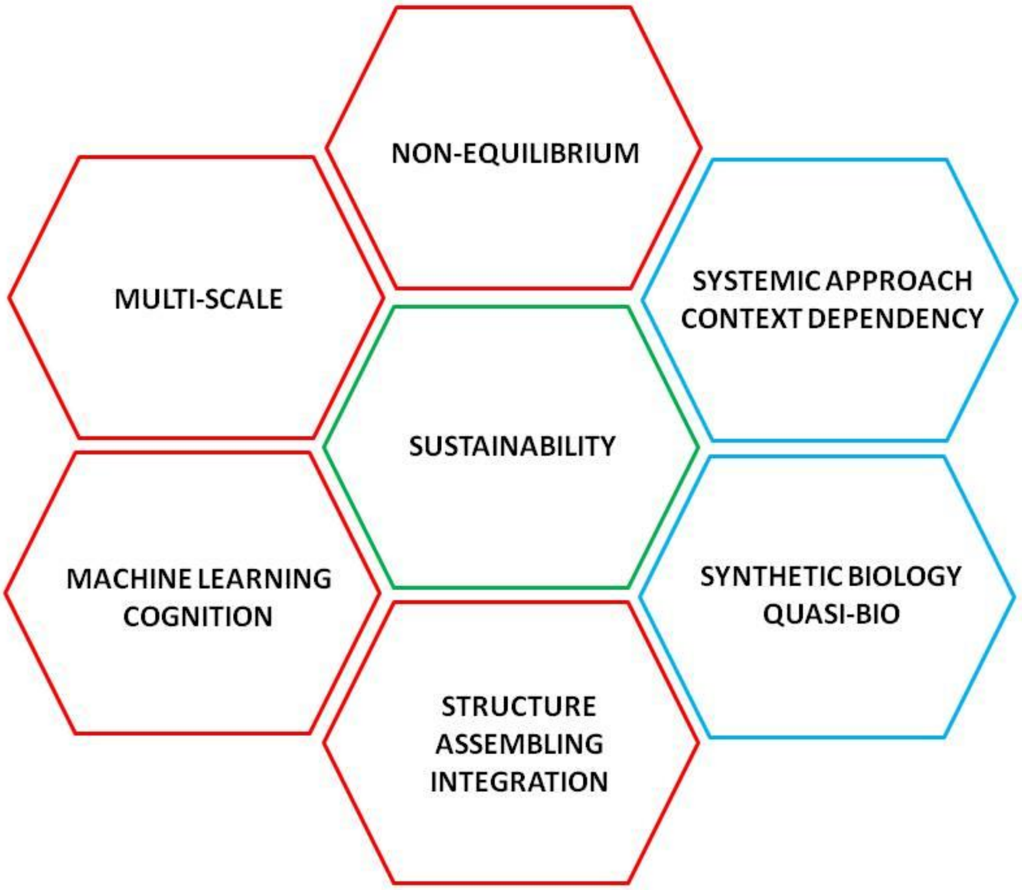

Figure 1: a brief sketch of the aspects identified as those to be addressed for tackling the challenge of stem materials. In blue, those which at the moment seem to be closer to biology, in red those which are mainly framed in physics, material and computing sciences, and in green the aspect of sustainability 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
3. Hoffmann C.M., Rossignac J., 1996, "A road map to solid modeling", IEEE Trans Vis Comput Graphics, 2(1), 3
4. 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. Nanotech*nology, 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 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