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NEWS

Synthetic biology leading to specialty chemicals

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Synthetic biology can combine the disciplines of biology, engineering, and chemistry productively to form molecules of great scientific and commercial value. Recent advances in the new field are explored for their connection to new tools that have been used to elucidate production pathways to a wide variety of chemicals generated by microorganisms. The selection and enhancement of microbiological strains through the practice of strain engineering enables targets of design, construction, and optimization.

Pathway analysis leads to a comprehension of how chemicals can be produced by these novel synthetic systems. New synthetic biology tools provide an assessment of the current developments leading to commodity chemicals, specialty chemicals, pharmaceuticals, and nutraceuticals. A synthetic biology toolbox offers a means to harness the essential capacity of organisms by diverting metabolic resources into the production of diverse and renewable specialty chemicals. The field is quickly shifting from a paradigm of increasing endogenous production which has dominated the field. Currnetly, simple discovery offers the opportunity to identify pathways contributing to a new paradigm marked by fully, rationally designed circuits and synthetically designed/optimized pathways. Recent developments of biotechnological techniques and models directed to the understanding and manipulation of metabolism and gene expression are summarized. These synthetic biology tools are organized according to their primary function: for the design, the construction, or the optimization of a pathway. The importance of these tools can be demonstrated for their contribution to the production of chemicals and has identified a diverse set of organisms to be exploited by the application of metabolic engineering.

Monomers such as styrene have been identified as candidates for new technology development due to their intensive energy requirement for production. A de novo synthetic design utilizes a novel metabolic pathway using glucose as a renewable feedstock. Deriving polymers and copolymers directly from microorganisms becomes possible. Polylactic acid (PLA) having low toxicity to humans and high biocompatibility is a well-known macromolecular, biodegradable target. Recent research shows PLA to be available from an *E. coli* strain with a molecular weight of 141,000 Da at a titer of 20 g/L.

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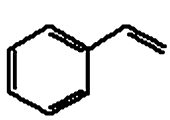
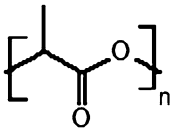
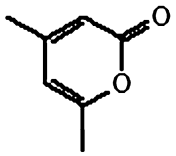


Styrene



Polylactic acid



4,6-dimethyl-2*H*-pyran-2-one
(Triacetic acid lactone)

Commodity Chemicals

The interface of synthetic biology with metabolic engineering offers many yet to be explored opportunities. Chemical toxicity remains a major hurdle to future progress in the field of synthetic biology. Synthetic biology techniques continue to provide the basis for expansion to a broader field of candidate microorganisms along with improvements to titer and yield. A host of new chemicals derived from this technology is expected to accelerate and provide industrial scale processes comparable to those of the current petrochemical industry.

Annu Rev Chem Biomol Eng 2015, 6, 35–52, Biotech Adv 2016

Chemical footprint analysis for safer chemical use

Guidance is now available to aid interested parties to assess the ability of companies to manage chemicals. A corporate *Chemical Footprint* establishes a baseline from which a company can measure the effectiveness of goal setting actions designed to reduce the use of chemicals of high concern and the development and use of safer alternatives. The 45 page report *Guidance for Using the CFP Assessment Tool* is easily available from the sponsoring *The Chemical Footprint Project* site. The move to safer chemicals can assist companies develop new forms of transparency and show new efforts to enhance their reputation through new abilities to address risks and exploit opportunities available through the use of safer chemicals. The assessment tool enables the evaluation of companies in four areas: chemical inventory recognition and completeness, management support and strategy, capability to measure corporate progress, and the effectiveness of communication through public disclosure.

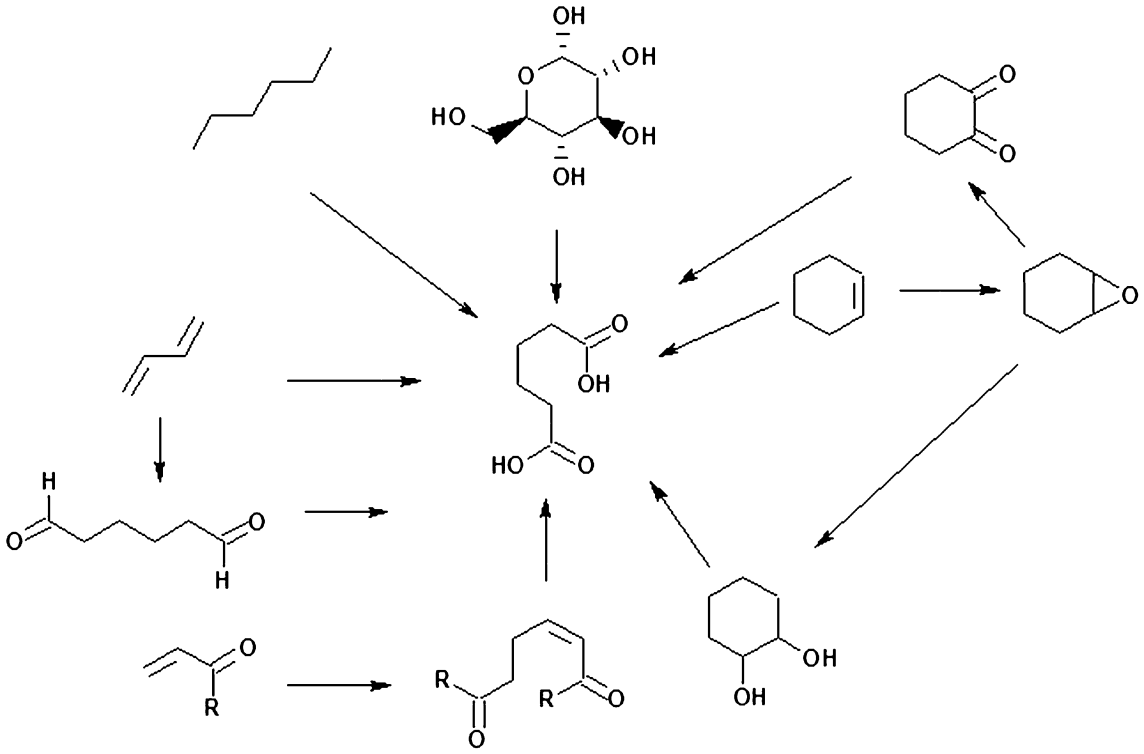
The footnote analysis is based on the use of 19 questions selected to evaluate corporate measurement in terms of the advocated chemical policies. The integration of those policies with business strategies, the level of knowledge held by a company about the chemicals in its products, components, and manufacturing processes, the extent to which a company achieves goals it sets to reduce chemicals of high concern, and the extent to which a company publicly releases information about the chemicals in its products and manufacturing processes contribute to the question formulation.

The environmental non-profit *Clean Production Action*, The Lowell Center for Sustainable Production at the University of Massachusetts Lowell, and the sustainability consultant firm Pure Strategies have organized *The Chemical Footprint Project*. The mission of this effort is designed to transform global chemical use by measuring and disclosing data on business progress to safer chemicals. The project website affords opportunities to interested parties to access the report and conduct the application of the Chemical Footprint evaluation to their company.

https://www.chemicalfootprint.org/assess

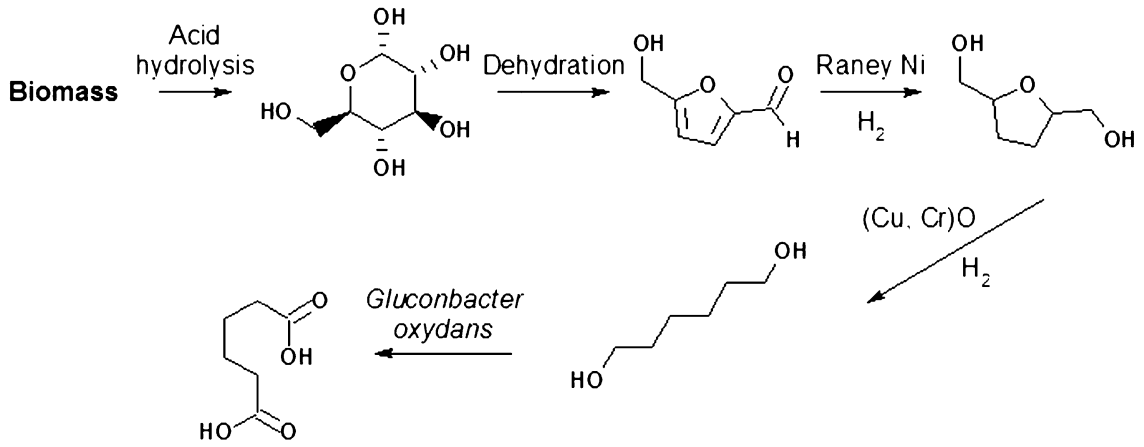
Moving to bioadipic acid

Important commodity chemicals such as the six carbon diacid, adipic acid are becoming targets for synthetic technology innovation to improve the process environmental footprint and to utilize biobased pathways using renewable materials. Traditional processes leading to the manufacture of adipic acid involved industrially aged chemistries and unsustainable multistep processes. Homogeneous catalysts, strong oxidants (e.g. concentrated nitric acid) led to the production of large quantities of nitrous oxide which is a greenhouse gas. Over the past 70 years, extensive research has been conducted to develop alternative and cleaner process routes to adipic acid, a variety of raw fossil materials with new oxidants, catalysts, and reaction conditions have been exploited to formulate improved reaction schema to avoid obvious elements of environmental pollution. Early life cycle studies have emphasized the importance of bioprocesses utilizing materials derived from different components of biomass. Biobased synthetic approaches have been commercially pursued utilizing renewables, such as glucose or vegetable oils as starting materials.



Chemical routes to adipic acid

Biobased reaction pathways are considered to be more benign than the traditional petrochemical approaches. Biologically based processes synthesizing adipic acid can utilize various combined fermentative/chemo-catalytic or fully enzymatic biotechnologies. Results look promising leading to the expectation that adipic acid from a bio-based process could be a market component in the next few years.



Biobased synthesis of adipic acid from biomass

Ind Eng Chem Res 2015, 54, 1–46, 567–576

Weather-related disaster as human cost

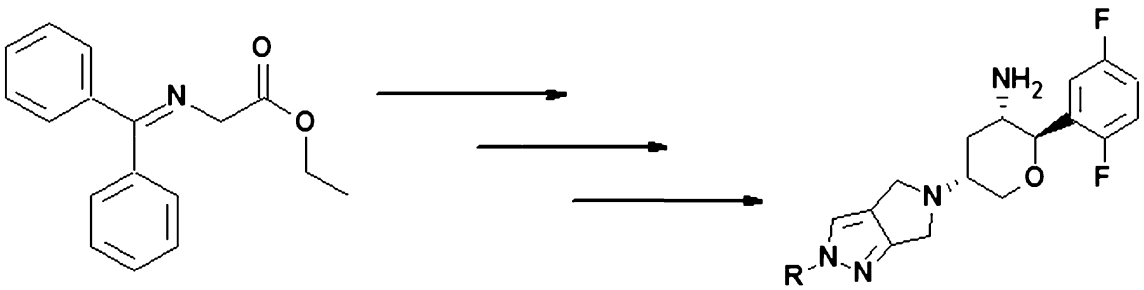
Weather conditions such as floods, storms, heatwaves, and other weather-related events of the last 20 years have triggered the majority (90 %) of disasters across the globe. The widely recognized international EM-DAT database has tabulated some 6457 weather-related disasters worldwide. Weather-related disasters during this period account for 606,000 deaths or about 30,000 per annum. An additional 4.1 billion people were injured, left homeless, or in need of emergency assistance.

Frequent weather-related disasters are connected with a rise of floods and storm occurrences. Flooding contributed 47 % of all weather-related disasters in the timeframe 1995–2015 with a geographic focus in Asia affecting 2.2 billion people. Storms were less frequent but the most deadly type of weather-related disaster leading to the death of more than 242,000 people over the past 21 years. Lower-income countries saw the vast majority of these mortalities despite experiencing 26 % of all storms. Weather extremes (e.g. extreme cold or heat waves) were found to be rather deadly for each event. Income differences for the countries studied exhibit a range of effects. Weather-related disasters for the period of 2005–2014 were found to have increased by 14 % in contrast to the 1995–2004 timeframe. The two critical factors of population growth and uncontrolled building on flood plains and storm-prone coastal zones will increase exposure of human populations to extreme weather events. Analysis of the EM-DAT data suggests that an economic cost of $1891 billion US but is expected to rise with more complete analysis of weather economic losses. Reporting gaps emphasize the need for robust and well-maintained national disaster loss databases to provide a better loss analysis. The report shows that economic losses from weather- and climate-related disasters have been heavily influenced by increasing exposure of people and economic assets. Application of proactive management at several levels could save more lives in the future.

http://www.unisdr.org/2015/docs/climatechange/COP21_WeatherDisastersReport_2015_FINAL.pdf

Chemical manufacturing route evolution

Selection of chemical routes to a desired chemical or pharmaceutical requires considerable scrutiny to ensure the development of a process route that is safe, efficient, and economical yielding pharmaceuticals having high conversion and high purity from reasonably accessible starting materials. One example of such an undertaking can be found in the development of a manufacturing route to omarigliptin which is a long-acting treatment for Type 2 diabetes. The utility of dipeptidyl peptidase-4 (DPP-4) inhibitors as a treatment therapy for type 2 diabetes was successfully demonstrated through the commercialization of sitagliptin. The worldwide Type 2 diabetes epidemic involves more than 366 million with a population of almost 26 million in the US alone. Driven by a desire to reduce the dose and increase the therapeutic half-life for the Type 2 diabetes treatment pharmaceutical, a new search was aimed at the elucidation of new diverse potent drug candidates. Omarigliptin was found to be a highly functionalized and structurally differentiated long-acting DPP-4 inhibitor.



Omarigliptin

Generalized concept for omarigliptin synthesis

The target molecule is synthesized via the diastereoselective reductive amination of a pyranone through a mesylated pyrazol followed by BOC group deprotection. Ruthenium catalysis was used to accomplish three steps of the manufacturing process. The 1st is the Dynamic Kinetic Resolution reduction of a *rac*-α-aminoketone which set the orientation of two contiguous stereogenic centers. The 2nd accomplishes a cycloisomerization of a bis-homo propargylic alcohol to a dihydropyran. The 3rd converts a pyranol to the desired pyranone through Ru-catalyzed oxidation. This sequence avoided the handling of a mutagenic salt with improved overall diasteroselectivity efficiency of the manufacturing route. The overall yield starting with the glycine ester is 29 %.

Org. Process Res. Dev., **2015**, *19* (11), pp 1760–1768

Mountaintop removal

An environmental non-profit organization Appalachian Voices recently released an important report *Communities at Risk from Mountaintop Removal* which depicts and analyzes the effects of mountaintop mining in central Appalachia which uses 30 years of satellite imagery and other information to depict the encroachment of these mining operations to communities of this region. Mountaintop removal coal mining is a technique whereby the non-coal-bearing strata generally closer to the surface is removed to access the rich coal-bearing seams found in this region.

The down side of coal production is easily recognized by the results of mountaintop practices which leave the area appearing as a moonscape with significant environmental pollution problems. The economic factors arising from coal company bankruptcies, mine layoffs, and steep declines in coal production complicate the picture. Competition with the newly discovered natural gas production from the Marcellus Shale formation has depressed coal production due to the attractive environmental features of natural gas for electricity production. The controversial use of mountaintop removal to access thin seams of coal uses explosives to blast the overburden tops off of mountains to access thin seams of coal. This mining practice has been shown to have a broad range of human and environmental impacts involving increased rates of cancer and birth defects for populations proximate to these mines, increased concentrations of chemical pollutants contaminating downstream water supplies, and the loss of a broad spectrum of aquatic organisms in mine-impacted streams. Many residents in Appalachian coal mining communities have recognized that large mountaintop removal mining operations continue to expand nearer to their homes and communities in recent years.

To help understand the extent of the threats Appalachian communities face from mountaintop removal the group, *Appalachian Voices* undertook a research project to identify the current relationship between mountaintop removal and the communities in the region where it occurs. A novel dataset was developed using geospatial analysis tools to detect and map mining activities across a 30-year timeframe using satellite imagery for the Central Appalachian coal mining region. The dataset was combined with a U.S. Board on Geographic Names database of populated places to decide whether mining had moved closer to Appalachian communities recently, and to classify 50 communities having the greatest recent encroachment of large-scale mining activities. The U.S. Census Bureau data were used to analyze demographic and economic trends and to compare trends in rural communities of the same counties having no surface mining activities nearby with the 50 selected "at risk" communities.

Mountaintop removal continues to encroach on communities of Central Appalachia which encompasses three states and 23 Central Appalachian counties. The report shows that communities having surface mine encroachment increases suffer greater rates of poverty and population loss is twice as fast as nearby rural communities with no mining in the immediate vicinity. The search of high-quality metallurgical coal has identified communities where the threat of mountaintop mining encroachment is very real in current and future timeframes particularly for southern West Virginia.

http://appvoices.org/resources/reports/Communities_At_Risk_from_mountaintop_removal_April2015.pdf

Reinventing chemistry

Chemistry is one of the supporting foundation scientific elements required for the development of clean technology. In a recent essay, George Whitesides of MIT mused on the past, present, and future of chemistry as foreseen through a remarkable analysis. The occasion for this analysis was the recent celebration of the 150th anniversary of operation for the German chemical giant, BASF. The essay traces developmental paths of the past and projects the patterns to possible futures. The demands of understanding for large systems often governed by living biology require an abrupt change from the established manipulations of small molecules and reactions.

The study and use of chemistry is in a period of change, from a past era characterized as focused on molecules and reactions, to one in which manipulations of systems of molecules and reactions will be essential parts of controlling larger systems. Earlier directional foci were supported as a matrix of interests evolving from university research to the interests and support of industry, government, and

taxpayers. Discovery partners were developed through inter-university and inter-government arrangements which led to significant discoveries and advances. For corporations, research as a long-term investment is now considered an expense. With these perspectives as a backdrop, the future is thoughtfully outlined. Clearly, changes are anticipated and the future can be seen as a more complex challenge when compared to the past. The author offers an answer to the question of "What's next" in the form of 24 classes of new problems where chemistry is expected to strongly contribute to the solutions. The new classes range from issue of the molecular basis of life to the chemistry of planets to new areas of science opened by new analytical techniques. The utilitarian nature of chemistry continues to offer new and far-reaching applications beneficial to society. Clean technology is but one very important area where chemistry can be expected to provide new vistas to solve problems of material production and environmental pollution.

Angew Chem Int Ed 2015, 54, 3196–3209

Importance of clean environments to disease prevention

Each year an estimated 12.6 million deaths are found to be caused by unhealthy environments. Almost 25 % of total global deaths are attributable to these causes. Air, soil, and water pollution along with other environmental risk factors (such as chemical exposures, climate change, and UV radiation) directly impact injuries and more than 100 diseases. The largest share of environmental-related mortalities can be ascribed to non-communicable diseases (NCDs). The World Health Organization has recently released the 176 page 2015 edition of their "*Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks*" report. NCD deaths are generally attributable to air pollution (including second-hand tobacco smoke exposure), resulting in 8.2 million deaths. Contributors such as stroke, heart disease, cancers, and chronic respiratory disease, caused by unhealthy environments currently account for almost two-thirds of the total deaths. Infectious disease deaths (e.g. diarrhea and malaria), traceable to poor water quality, sanitation, and waste management, have declined. Accessibility to safe water and sanitation have been identified as main contributors to this decline, complemented with improved access to immunization, insecticide-treated mosquito nets, and essential medicines.

It is broadly recognized that a healthy environment is a basic necessity for a healthy population. Where the necessary changes are not made to provide a healthy environment, the mortalities will continue with the populations dying too young. For the increasing trend of environment-related disease and deaths to decrease, countries must provide support in the form of know-how (such as low-carbon technologies) and reduce the use of solid fuel use for cooking.

Environmental risk reduction is key to developing protective responses to injurious conditions of our workplaces, homes, and cities. Investment in strategies designed to curtail the implicated environmental risks can significantly reduce the increasing global burden related to cardiovascular and respiratory diseases, cancers, and bodily injuries with a healthcare cost savings that could enable broad implementation.

A survey of more than 100 disease and injury categories finds that cardiovascular diseases, such as stroke and ischemic heart disease account for the vast majority of environment-related deaths (Table 1).

Young children and older people are well recognized as the vulnerable parts of society. Without action by the countries with susceptible populations, large segments of the populace will become ill and die in their youth. Non-communicable diseases account for the largest population susceptible to environment-related deaths.

Geographically, low- and middle-income countries of South-East Asia and the Western Pacific have exhibited the largest 2012 environment-related disease burden of a total of 7.3 million deaths generally attributed to indoor and outdoor air pollution (Table 2). All types of diseases and injuries can be found distributed through relatively high to high-income countries.

Healthy environments lead to a healthy population. The report asserts that cost-effective processes are available to assist attempts to reverse environmental diseases and deaths. Strategies to improve the environment and disease prevention have been established to prevent and reduce

Table 1 Yearly leading causes of death

Leading cause	Deaths per annum (millions)
Stroke	2.5
Ischaemic heart disease	2.3
Unintentional injuries (traffic deaths)	1.7
Cancers	1.7
Chronic respiratory diseases	1.4
Diarrheal diseases	0.846
Respiratory infections	0.567
Neonatal conditions	0.27
Malaria	0.259
Intentional injuries (i.e., suicide)	0.246

Source WHO (2015) Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks. Geneva, pp xv–xvi

Table 2 Geographical death dependence

Geographical regions	Deaths per annum (millions)
Africa	2.2
Americas	0.847
Mediterranean	0.854
European	1.4
South-east Asia	3.8
Western Pacific	3.5

Source WHO (2015) Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks. Geneva, pp xviii–xxi

acute respiratory infections, chronic respiratory diseases, cardiovascular diseases, and burns. Clean technologies and fuels for domestic cooking, heating, and lighting are offered as solutions. Clearly, indoor and outdoor renovations of current practice will assist the attainment of the projected goals.

http://www.who.int/mediacentre/news/releases/2016/deaths-attributable-to-unhealthy-environments/en/

The effect of full electric transportation for the environment

The Electrical Power Research Institute (EPRI) and the National Resources Defense Council (NRDC) have recently published the interesting 100 page report titled: *The Environmental Assessment of a Full Electric Transportation Portfolio*. This analysis looks to identify the potential impacts of an anticipated shift of energy use for transportation to electricity with the expectation that electricity will eventually replace about 50 % of projected light- and medium-duty transportation fuel use and a significant portion of non-road–fuel use. As a complement and extension of a 2007 report, *Environmental Assessment of Plug-in Hybrid Electric Vehicles*, the 2015 report offers an expansion to include impact analysis of two aspects of electric transportation. The analysis of the greenhouse gas emissions from 2015 to 2050 and the analysis of air quality impacts in 2030 show plug-in hybrid electric vehicles could both contribute to significant reductions in national greenhouse gas emissions and also lead to improved air quality. Recent emission trends and a discussion of best practices for modeling large-scale changes in electricity-sector load show wide variation of emission rates.

Projections of the grid emissions attributable to use of electricity as a transportation fuel need to be modeled. Grid-Modeling and Load Modeling efforts need to be expanded. Uncertainty analysis will be needed across the entire system of inquiry. These new transportation components continue to look promising and there is a large support effort backing their success.

http://www.epri.com/abstracts/Pages/ProductAbstract.aspx?ProductId=3002006881

New journal

A new trans-disciplinary, open-access journal, *Elementa: Science of the Anthropocene* seeks to publish original research reporting new information and knowledge concerning the Earth's physical, chemical, and biological systems. Coverage of the interactions of human and natural systems are important components to this area of research along with the elucidation of steps relating to the mitigation and adaptation to global change. This journal looks to facilitate collaborative, peer-reviewed research leading to accelerated scientific solutions to challenges of this era of human impact.

This non-profit, peer-reviewed journal is a derivative of a unique collaboration among a group of collaborators involving BioOne, Dartmouth, the Georgia Institute of Technology, the University of Colorado Boulder, the University of Michigan, and the University of Washington.

The following types of manuscripts are sought research article, policy bridge, practice bridge, commentary, comment & reply, and book reviews. In addition to the traditional publishing venues, the journal looks to assist authors who present their work in a particularly engaging way, offering the opportunity to display additional materials such as slideshows and videos alongside their research; and making all articles available in multiple formats such as PDF, HTML, EPUB, and Mobipocket. Thematic issues are welcomed and can be assembled from a set of papers addressing themes or projects of broad interest, typically 4–10 articles in each group, usually including a synthesizing commentary.

http://elementascience.org/