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The scope and scale of the life sciences (‘Nature’s envelope’)

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Abstract

The extension of biology with a more data-centric component offers new opportunities for discovery. To enable investigations that rely on third-party data, the infrastructure that retains data and allows their re-use should, ideally, enable transactions that relate to any and all biological processes. The assembly of such a service-oriented and enabling infrastructure is challenging. Part of the challenge is to factor in the scope and scale of biological processes. From this foundation can emerge an estimate of the number of discipline-specific centres which will gather data in their given area of interest and prepare them for a path that will lead to trusted, persistent data repositories which will make fit-for-purpose data available for re-use. A simple model is presented for the scope and scale of life sciences that includes all of the processes conducted by or caused by any and all organisms. It is depicted on a grid, the axes of which are (x) the durations of the processes and (y) the sizes of participants involved. Both axes are presented in \log_{10} scales, and the grid is divided into decadal blocks with ten fold increments of time and size. Processes range in duration from 10^{-17} seconds to 3.5 billion years or more, and the sizes of participants range from 10^{-15} to $1.3 \cdot 10^7$ metres. Examples are given to illustrate the diversity of biological processes and their often inexact character. About half of the blocks within the grid do not contain known processes. The blocks that include biological processes amount to 'Nature's envelope', a valuable rhetorical device onto which subdisciplines can be mapped, and from which can be derived some key requirements for a comprehensive data infrastructure.

Keywords

Nature's envelope, scope of life sciences, scope of biological sciences, cyberinfrastructure, macroscope

Background

The growth of a data-rich and data-centric aspect of biology brings the prospect of new opportunities for discovery – both generally (National Research Council of the National Academies. 2009, National Science Foundation Cyberinfrastructure Council. 2007, National Science Foundation Office of Advanced Cyberinfrastructure 2020, OECD Megascience Forum Working Group on Biological Informatics 1999, Tansley and Tolle 2009) or in respect of particular disciplines (e.g. Hobern et al. (2019), Jones et al. (2006), Parr et al. (2012)). Data-mining adds to the processes of deduction, induction, guesswork, reductionism, and experimentation; it may reveal new patterns, better describe known patterns, or direct attention to informative outliers. With associated improvements in computing power, it enables analyses that require so much data that they were previously impractical. Access to large quantities of data may reveal patterns that were not discernible before, and stabilizes less certain insights. With appropriate interoperability, previously isolated disciplines can be interconnected to explore processes that extend across multiple scales. In many regards, the potential of a framework, toolkit, and personnel trained to take advantage of this new growth in Biology closely corresponds with Joel de Rosnay's vision for a 'macroscope' – a device intended to analyse phenomena previously deemed to be too complex to allow any real progress (de Rosnay 1975).

The potential of data-centric developments will be realized best if scientists can call on an appropriate (cyber) infrastructure. Examples of existing environments include Genbank and the other members of the International Nucleotide Sequence Database Collaboration (Brunak et al. 2002, Federhen 2012, Karsch-Mizrachi et al. 2012) for molecular biology, and the Global Biodiversity Information Facility (GBIF) and the Ocean Biodiversity Information System (OBIS) for occurrence data (Heberling et al. 2021, Vanden Berghe et al. 2013). Such data aggregators can capture and standardize data, promote training and standards for new skill-sets, foster a shift in conventions towards data-sharing and re-use of data; and set priorities (Hardisty 2013, Thessen and Patterson 2011). Once in place, discipline-based aggregation centres lead to new tools and environments that have agendas beyond the initial intent.

The assembly of such environments for all domains of biology is a colossal challenge. It will be very costly and will depend on a new political commitment to fund the construction and persistence of the service infrastructure. Some argue that urgent science problems should be the driver for this new infrastructure (Stern et al. 2020). This would be a decentralized approach. It would favour particular agendas, be agile and responsive to needs; but it will also be part of the competitive research enterprise and will add to the fragmented character of biology. de Rosnay's macroscope perspective reminds us that a well-designed global cyberinfrastructure should enable progress not only with pressing agendas but also with less proximate concerns.

The position taken here is that the research environment is ill-suited to the assembly and maintenance of a persistent service cyberinfrastructure. Most research is based on short

term projects such that continued funding, and hence the persistence of the infrastructure, is not certain. Most current discipline-based repositories serve a particular research agenda, but lack the resources to ensure access to all data in perpetuity, provide quality control processes, or to prepare content for transfer to trusted data repositories. Without a commitment to capture all content, some legacy and at-risk information will not be made digital or not in forms that allow for easy analysis. Those data will simply be lost from inclusion in current and future scientific efforts. That is, we need to consider the needs of a comprehensive infrastructure without being constrained by what best serves trend-setters in current research.

The requirements for an ideal general-purpose (enabling) infrastructure are reasonably predictable. Using the term agent to refer to individuals, institutions, or programmes; it is expected that one or more agents will take responsibility for the discovery and aggregation of all data within each of all domains of research. The most inclusive stance should be taken as to what constitutes a domain of research. Sources should include the output of any project, individual, team, or programme; data collected by funding sources, institutions, publications, publishers, databases, computed data, and so on. Output from sources will be discovered and copied (aggregated) by agents into one or more data centres representing their defined domains of research. It is expected there will be more than 10,000 discipline-focussed data aggregators. As information may or may not have been 'born digital', devices will be need to ensure that legacy data are made digital. Once acquired, data will need to be normalized, have key provenance and discipline-specific metadata added; and then be made available through reliable and trustworthy pathways for harvesting by trusted data repositories that meet CoreTrustSeal standards and that guarantee access to the data in perpetuity (Corrado 2019, Dillo and De Leeuw 2018, Downs 2021). Compliance with FAIR principles (Wilkinson 2016) or more demanding standards is expected.

Some of the immediate challenges that an infrastructure will face are already evident from research in biology that relies heavily on the re-use of data. A good example is the re-use of molecular data in investigations of phylogenetic relationships (e.g. Hinchliff et al. 2015). Such studies reveal uncorrected misidentifications of material (e.g. Leray et al. 2019, Pentinsaari et al. 2020) or other errors in the data (Bidartondo 2008). A second challenge is the integration of information from different sources. This problem arises in broad cross-discipline areas (Jones et al. 2006, Miled et al. 2004, Nishant et al. 2011), within subdomains (Hall et al. 2013), for taxonomies (Franz and Sterner 2018, Garnett et al. 2020), or even in the very narrow domain of occurrence data (Belbin et al. 2013, Mesibov 2013). Immediate problems may misdirect attention from the absence of a clear plan and protocols that will guide all data along the pathway from source to trusted repositories of fit-for-purpose data.

Along the pathway from source to repository, at least one agent will need to take responsibility for polishing services that will correct errors, keep metadata up to date, update software-dependent data, correct flaws in aggregation processes, and so on (Belbin et al. 2013, Mesibov 2013, Franz and Sterner 2018). Without this, there can be no guarantee that data will be fit for purpose. Such polishing services include those needed

for scientific names because errors and idiosyncrasies with names are common in data sources (Patterson et al. 2016), despite the very high significance of names as metadata. Names and associated taxonomic concepts (identities) change with new research in nomenclature, systematics, and phylogeny; such that the prior use of names may need to be updated. That is, it must be assumed that any name strings associated with or acting as a data object may need to be corrected or replaced on one or more occasions. With appropriate investment, name polishing can be provided through on-line reconciliation and resolution services (Mozzherin et al. 2017, Patterson et al. 2010). Older occurrence data may need polishing to maintain currency with geopolitical developments. The pathway should include annotation services such as Filtered Push (Wang et al. 2009) which allow users and curators to add comments or corrections and hence improve the quality of data.

A service-oriented infrastructure must include, and be built atop, a foundation layer of discipline-based aggregators. Absent from discussions about a general cyberinfrastructure is an assertion of the full extent of the life sciences. Such an assertion is needed to guide planning efforts with estimates of the number of data sources, the amount and character of primary data, requirements for discipline-specific data aggregation and management centers which will deliver fit-for-purpose data to persistent repositories with curatorial practices that meet the highest standards (Dillo and De Leeuw 2018, Downs 2021). Without recognition of the scope and scale of the discipline, the costs of building an infrastructure will not be known, the political will for new funding models will be absent, and the enabling cyberinfrastructure that some seek will not emerge.

Nature's Envelope

The intent here is to establish the scope and scale of biology as a contribution to the realistic planning for a data infrastructure that can serve all aspects of the biological sciences. All life is a single array of processes which are interconnected from the molecular level to the global. Each process can be represented by the size(s) of the participant(s), and its duration. Arguably, process-based metrics can be applied to any facet of biology, unlike metrics based on 'objects' – such as the number of species or other measures of biodiversity, the number of data objects, or the number of agents (Thessen and Patterson 2011). The emphasis on process is useful as processes are the targets for most discovery efforts.

The framework for this exercise was a grid with \log_{10} axes for duration of processes in seconds and the size(s) of participants in metres. The choice of using a log scale is one of convenience only and is consistent with other efforts to represent information that extends over broad scales (Morrison and Morrison 1994, 't Hooft and Vandoren 2014). The approach has been applied in more limited extents to biology (e.g. Buonomano 2007, McGeogh 1998).

The result (Fig. 1) was a grid that extends across about 35 orders of magnitude of time, and about 21 orders of magnitude for size. Instances of processes were taken from all

levels of organization and were plotted onto this framework, selecting those decadal blocks (defined by their lower left corners) in which processes occurred. Examples of biological processes follow, and they were found to occur in about half of the available blocks. A line was drawn around the examples to give the green area in Fig. 1. The periphery was blurred to reflect the inexact metrics of processes. The green area is 'Nature's Envelope'.

As biology merges with chemistry, physics, geology and other sciences, it is helpful to indicate what was included in this exercise to establish the outer bounds of the life sciences. Inclusion is limited to processes conducted by, in, or among living organisms, and the consequences of those processes. The result is not theoretical, but is a summary of processes that embrace subatomic events, molecular and biochemical events, cellular, tissue, organismic, ecological, evolutionary, and global events. Most are obviously active processes: examples being the acquisition and translocation of ions, transformational changes in motility proteins such as myosin or kinesin; the flight patterns of peregrine falcons, or the expansion of ground cover by colonial plants. Some verge on being considered passive: such as the passage of photons through chlorophyll molecules, but this is included as there is an active component that intercepts and retains energy. Also included is the expansion of the oxygen-containing atmosphere, as it is driven by photosynthetic processes. The expansion of the distribution of invasive species is included, but the movement of the virulent B.1.1.7 COVID strain aka VUI – 202012/01 recorded in Britain in October 2020, and located in the US and Australia in December of the same year is not (because of the involvement of air travel). The course of Voyager spacecraft, the ages of inert fossils, and the fossilization process are not included. Clearly, inclusion of processes as 'life sciences' is open to debate and may need to be reset with future versions of Nature's Envelope.

The emphasis on processes involves an unfamiliar inexactness in information. Processes are transient by nature, are influenced by other processes, internal and external environments, recent histories, age, the number and diversity of directly or indirectly connected participants, whether information is obtained in vivo, in vitro, by inference or calculation, and so on. As an example, of the imprecision involved, the time it takes for mRNA to move from a nucleus to the outer margins of a cell depends on the number of nuclear pores, the size of the cell, whether cyclosis is expressed and how, by temperature, whether the mRNA is remodelled into a ribonucleo-protein or not, involvement of molecular motors, the alleles available within the observed population, the species, and the type of cell. Consequently, the speed of movement varies by at least two orders of magnitude (Rodriguez et al. 2007). Rather than represent processes by exact numbers such as a mean value, the construction of the first draft of the 'Nature's Envelope' graphic used minimal and maximal estimates of range.

The extremes of the envelope that includes all life processes was set by identifying the processes with shortest and longest durations, and those with the smallest and largest participants. The briefest process is the interception of a photon by a photopigment molecule during which energy is transferred from the photon to the photopigment. A photon of light travels at 300,000 km ($3 \cdot 10^8$ metres) per second. A chlorophyll molecule measures about 2-3 nm or $3 \cdot 10^{-9}$ metres. A simple calculation establishes that the amount of time that

a chlorophyll molecule is exposed to and must take advantage of the energy of a photon is 10^{-17} seconds. As for the size of the participating photon, the treatment of photons as objects with size is questionable, but there is a consensus that a size of 1.10^{-15} m is appropriate (Pohl et al. 2016). The process used for the other extreme is that of evolution, for which we use as a start point the oldest recorded fossils of bacterial stromatolites which date back to about 3.4 – 4.2 bya (Dodd et al. 2017). The evolutionary process has therefore endured for about 10^{17} seconds. The participant in the evolutionary process is Earth. The size is taken as the solid mass plus 100 km depth of oxygen-influenced atmosphere, that is, about 13.10^6 m.

To meet its objectives, the attempt was made to map sample biological processes into decadal blocks within the grid. As an example, [the process of a \(dead\) whale exploding](#) from pressure of gasses accumulating in its intestines endures for about 1 to 10 seconds and involves an object about 10 metres long. As with all other processes, this is not isolated. It is interconnected with the metabolism and growth of individual bacteria, populations of genetically similar organisms, and taxonomically diverse communities all of which contribute to the production of the gases. The eruption is also connected to responses by members of the microbial food web and other scavengers that benefit from the resulting supply of dissolved and particulate food materials.

Three classes of further examples illustrate the process by which the envelope was populated, and reveal more of the problems that were encountered.

Life history data are included for all classes of organisms, from sub-micron viruses to honey fungi and tree clones extending over multiple kilometres. Examples with short and long life-spans were favoured. Data on the generation times of identified bacteria measured in minutes, to various species of trees known to be many thousands of years old were included. Examples were mapped onto decadal blocks using the size-range of individuals of the relevant species. Times of early demise and fossilization processes were not included. Data on life-spans were extended to classes of cells. The doubling times of many protists (single cells) are known and some were included. The life-spans of human red blood cells populate two decadal blocks. Both are defined by the size 1-10 μ m (red blood cells are 7-8 μ m in diameter), but given that red blood cells can survive for 70-140 days, two blocks (defined by 10^6 and 10^7 seconds) were selected (Franco 2012). More blocks will be populated when a greater diversity of cells and organisms are included. The life-span concept was extended further to molecules. The life of mRNA molecules of some organisms has been measured, but, despite being expressed as half-time decay rates (Baudrimont et al. 2017), can be included.

A second class of examples relate to movements. Included are the increases in dimensions of organisms from nascent form to adult. An entry for growth of stromatolites is based on estimates of a few millimetres expansion per year. For some, data are entered for a species (Arctic terns migrate more than 10,000 kms in 3 months); while others and preferred are particularized. [Joe](#), a tumbler pigeon, departed Oregon (USA) on October 29th, 2020, and arrived 17,000 kms distant in Melbourne (Australia) on December 26th, 2020. Some activities are represented by more than one entry. Murmurations of starlings

are included both in decadal blocks defined by the size of individual organisms, and in blocks for the whole flock. Cyclical movements include the molecular motor kinesin that steps 10 nm or so in 100 microseconds as well as movements of organisms from bacteria to large trees in response to tidal, diurnal, lunar, seasonal, or annual cycles. Emergence events of *Magicalada* that are separated by many years are included. Movements in response to environmental factors, optimising location or orientation relative to directional factors (sunlight) or to gradients (such as the responses of microbial and meiobenthic communities to REDOX gradients) are included. Range extensions are included. Cane toads were introduced to North Queensland (Australia) in 1935 with the intent of controlling pests in sugar cane crops have since expanded their range by over 1000 kms. Entries for plants include the estimated 14,000 – 80,000 year period that the Pando clone of aspen trees has extended about 5 km (DeWoody et al. 2008).

The last suite is much of a miscellany. The envelope includes transactions, such as steps in metabolic pathways, the exchange of neurotransmitters between nerves, communications internally involving hormones, or externally involving pheromones. Microbial biogeochemical activities which are associated with transformations and precipitations of organic and inorganic deposits, including fool's gold (Thiel et al. 2019) or real gold (Reith et al. 2007) proved difficult to categorize. Some aspects of adaptation and evolution are included. The length of time involved in the acquisition of new behavioural traits, such as the ability of crows to use vehicles to break nuts, has been asserted (Nihei and Higuchi 2001). It is included using decadal blocks defined by the size of individual crows. Our recent experience with COVID also provides data on the emergence and spread of new genotypes, something that can be added to more conventional evolutionary trees with their asserted timelines.

Concluding comments

'Nature's envelope' (v. 1) is not intended as an analytical tool, but as a rhetorical device. Such devices have had a significant impact on the development of our discipline. Examples include the depiction of evolutionary relationships, the concept of evolution, so-called 'laws' like Gause's Law of competitive exclusion or Bergmann's Rule that within a clade those species that live in colder climes are larger, and various models from molecular to ecological that seek to represent reality. Although such devices may lack numeracy and exactness, they can be treated as testable hypotheses, and can grow into or spawn more exact assertions.

As a rhetorical device, Nature's Envelope aims to provide context for a diversity of conversations. Initially, it was motivated by the challenges of building a unifying informatics framework that might serve as the 'macroscope' that could aid the study of complex and interconnected issues in biology (de Rosnay 1975). More particularly, 'Nature's Envelope' can help to determine the number of discipline-based data aggregation centres that will be needed to discover, standardize and move data from primary producers into an environment where they may be freely used in computational analyses. At this time, there is not the political will nor resources to craft, build, staff and maintain a service-oriented

array of data services. For at least the time being, developments are likely to be driven by particular research agendas (Sternier et al. 2020).

The Envelope can be made more informative by the addition of layers. Fig. 2 includes a window that outlines which processes can be directly observed by a generalized individual. It allows for the formation of visual images after less than 0.1 second of exposure to a subject, and the capacity to discriminate items less than 0.1 mm in size. The upper right corner of the window uses examples of 19th century naturalists like Joseph Banks or Alfred Russel Wallace, whose decades of observations around the world led to insights on global distributions of plants and animals (the Wallace Line being a case in point).

Other layers may be developed to show which areas of biology benefit from particular technologies – such as how the individual experience window can be expanded by access to microscopes. Layers may inform us about the use of technologies or reveal which processes are measurable and which processes must be inferred. Layering can show where communities with particular taxonomic (or other specific discipline skills) can add information. Layering exercises that identify subdisciplines and the targets of special interest groups, help to clarify opportunities and requirements for data interoperability. In turn, this helps to set requirements for data and metadata standards.

While the current iteration of Nature's Envelope' is data-based, it is inexact and incomplete. It is a preliminary assertion that needs to be fleshed out – ideally using an open collaborative community (a template is available as Suppl. material 1 to aid this process).

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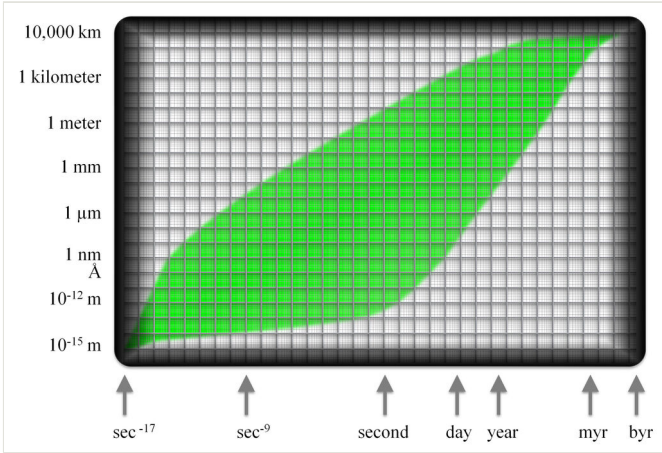


Figure 1.

The envelope that contains all biological processes. The axes are (horizontal) the duration of processes, and (vertical) the size of the participants. Metrics are represented in log₁₀ scales. The green area is where biological processes occur, and its periphery is 'Nature's Envelope'.

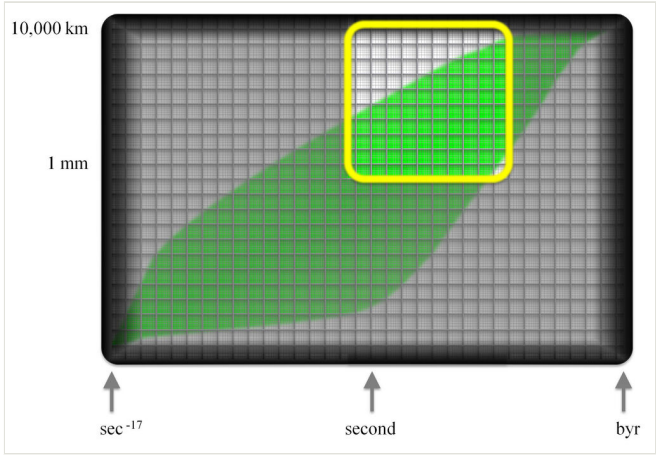


Figure 2.
'Nature's Envelope' with an added layer that shows the extent of living processes which may be perceived by a human individual.

Supplementary material

Suppl. material 1: Patterson Nature's envelope (template)

Authors: David J Patterson

Data type: Powerpoint

Brief description: A powerpoint file with an image of Nature's Envelope as submitted to RIO, with an additional editable layer as a window

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