Understanding spatial and temporal scale in biology

Wenfa Ng

Citizen scientist, Singapore, Email: ngwenfa771@hotmail.com

Abstract

Choice of temporal and spatial scale for querying biological systems is key to opening up nature's mysteries for investigation. For example, temporal resolution at which sampling is conducted is critical to answering granular details about a biological phenomenon, where a coarse sampling interval could not reveal fine level control on RNA transcription or protein translation. On the other hand, the spatial scale at which a biological question is posed concerns the validity of the conclusions drawn from the data obtained. Specifically, techniques and methods chosen for population level cellular assays would not be able to address questions at the single cell level, while the intricacies and caveats of single cell methodologies in understanding biological processes at the single cell level needs to be appreciated. More importantly, how single cell phenomena is aggregated to population level effects need to be factored into experiment design and data interpretation both for single cell and population studies. Specifically, as biology transcends multiple levels of organization ranging from single cell to clusters of cells and population, it is critical to gain understanding of how different biological effects could manifest at different population sizes. Hence, understanding the nuances of how temporal and spatial concepts could be deployed in experiment design in biology would help yield experiments that would more likely help address specific questions posed at the interface of subpopulations and subcellular level.

Keywords: biological complexity, temporal scale, spatial scale, biological organization, RNA sequencing, single cell, population level, subpopulations, sampling points,

Subject areas: biochemistry, cell biology, molecular biology, microbiology, bioengineering,

Perspective

Critical to designing appropriate experiments for answering specific questions in biology is a good understanding of time and spatial scale concepts. Specifically, time course experiments are important for correlating initiator-effector relationship between biomolecules in various cellular processes, while spatial scale is increasingly critical for gaining the appropriate understanding from experiments, whether at the population or single cell level.

Pulse chase experiments are one common tool for understanding the effect of an initiating event on a biological process. Thus, good understanding of the resolution at which a temporal question could be answered is critical to deriving the correct interpretation from experiment data. Specifically, knowledge of the relative timescale at which molecular events could be translated into macroscopic cellular behaviour is important; for example, how transcription of a mRNA could lead to a cellular response against viral infection, that ultimately results in cell lysis.

On the other hand, given the advent of single cell experiments and the experiment tools that supports it, an often neglected area of biological inquiry would need more careful consideration during experiment design. This concerns the level of biological organization pertinent to the question under consideration. More specifically, whether a population level or single cell approach is suitable for answering a question depends critically on the granularity and likely implications of the question. For example, RNA sequencing currently only works well at the population level, where RNA transcripts from all cells in the sampled population are pooled together for observing a hypothesized biological effect. However, what can we interpret from population level data and transpose it to the single cell level? From another perspective, how do single cell events aggregate to observable biological effect at the macroscale; for example, cellular differentiation or cell motility events?

Conversely, consider the emerging technique of single cell RNA sequencing. Take, for example, the desire to understand, at the single cell level, the relative contribution of cytosolic and mitochondrial proteins in assembling the oxidative phosphorylation pathway in single mitochondrion. Could single cell RNA sequencing of the RNA transcript provide a distinction between cytosolic RNA and mitochondrial RNA? The answer is yes, if it has the requisite sensitivity. Given the lack of sensitivity of the emerging technique of single cell RNA sequencing, it is currently impossible to apportion sampled RNA transcripts to specific subcellular fractions at the organelle level. Thus, understanding the spatiotemporal limits of techniques and instrument is important to appropriate choice of analytical tools from the biologist's toolbox during experiment design.

Hence, knowledge of the importance of time and spatial constraints to biological phenomenon is crucial for understanding experiment data derived, and more importantly, to the design of suitable experiments for understanding macroscopic phenomenon at a level of detail useful for yielding mechanistic knowledge detectable with contemporary techniques. Specifically, temporal scale is necessary for inserting time points into biological phenomenon under observation for demarcating initiation and lapse. Thus, using experiment tools and sampling points appropriately would help provide crucial verification of phenomenon hypothesized but non observable at a poorer resolution of temporal sampling; for example, understanding how fast cells react to the infusion of nutrients with a growth response.

At the spatial level, biological complexity remains the most neglected aspect of experiment design as graduate students are typically used to thinking at the population level in both designing and understanding experiments. More importantly, ability to transcend different organization scales such as the multitude of organizations between single cell and population remains a skill less practiced by students. Either population level or single cell, what about the in-between? Biological complexity spans many levels ranging from the single cell to an entire population in a shake flask, where do we start in asking a question is as important as the question itself. A single cell, a hundred cells or a ten thousand cells subpopulation, each with its own biology for investigation. Thus, ability to think in spatial scales at different levels, and more importantly, to relate between them is a crucial skill for the modeller and experimentalist.

Conflicts of interest

The author declares no conflicts of interest.

Author's contribution

The author thought about the importance of understanding temporal and spatial scale concepts to augmenting students' toolbox of concepts for understanding biology. He wrote to share his ideas with the biological sciences and bioengineering community.

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