Applied Category Theory for Genomics  
– An Initiative

Yanying Wu$^{1,2}$

$^{1}$Centre for Neural Circuits and Behaviour, University of Oxford, UK
$^{2}$Department of Physiology, Anatomy and Genetics, University of Oxford, UK

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Abstract

The ultimate secret of all lives on earth is hidden in their genomes – a totality of DNA sequences. We currently know the whole genome sequence of many organisms, while our understanding of the genome architecture on a systematic level remains rudimentary. Applied category theory opens a promising way to integrate the humongous amount of heterogeneous informations in genomics, to advance our knowledge regarding genome organization, and to provide us with a deep and holistic view of our own genomes. In this work we explain why applied category theory carries such a hope, and we move on to show how it could actually do so, albeit in baby steps. The manuscript intends to be readable to both mathematicians and biologists, therefore no prior knowledge is required from either side.
1 Introduction

DNA, the genetic material of all living beings on this planet, holds the secret of life. The complete set of DNA sequences in an organism constitutes its genome – the blueprint and instruction manual of that organism, be it a human or fly [1]. Therefore, genomics, which studies the contents and meaning of genomes, has been standing in the central stage of scientific research since its birth.

The twentieth century witnessed three milestones of genomics research [1]. It began with the discovery of Mendel’s laws of inheritance [2], sparked a climax in the middle with the reveal of DNA double helix structure [3], and ended with the accomplishment of a first draft of complete human genome sequences [4].

In the new era, with the advances in high-throughput sequencing technology and a flourish in bioinformatics, numerous details of various genomes have been accumulated. Consequently, a major challenge for the next generation genomics is to integrate those large amount of information, and to obtain a unified, global view of the genomes [5]. To address this challenge, various computational methods have been employed, including deep learning as the latest and most popular force [6,7]. Albeit missing from the list is applied category theory.

Category theory is a rising star in the pure mathematics field. It was invented for communication of ideas between different fields within mathematics [8]. Later people found that it is a language and mathematical tool that captures the essential features of certain subjects, and that it can be applied quite generally [9]. Category theory has already been successfully applied in computer science, linguistics and physics [10]. Actually, applied category theory has now grown into a brand new discipline itself, expanding territories into social science, cognition, neuroscience, cybernetics and many more [11].

In this manuscript, we propose that applied category theory is a powerful and perfect tool for the study of genomics. The main goal of this article is to explain why that is true. In order to do so, we will first introduce the history, current status and next big question of genomics. Then, we will describe briefly what is category theory and the current development of applied category theory, especially in biology. Finally, we try to bridge the two fields. Using the fly genome as a sample system, we demonstrate how applied category theory could help us better understand a genome as a whole.

Apparently our final aim: to uncover the organizational principle of genomes in general, is far from being reached in this initial work. However, with the right arms at hand and a clear direction ahead, all we need to do is to proceed. How about naming this course “Categorical Genomics” – a study of Applied Category Theory for Genomics?

2 Past, present and future of genomics

Genomics by definition is the study of all the genes of an organism, as well as their interactions with each other and with the environment. Genetics, on the other side, focuses on the function and heredity of single genes [12,13]. However, it is hard to draw a clear boundary between genomics and genetics; also genomics is closely intermingled with molecular biology and evolution. So, for the history of genomics, we take a subjective choice on what to cover, considering those relatively influential and relevant aspects but not restricted to genomics literally.
2.1 A brief history of genomics

The origin of genomics could date back to the mid 19th century, when Mendel’s laws of inheritance was first formulated in 1865. Mendel’s laws remained unnoticed and were later rediscovered independently by three scientists in 1900 [14]. Before Mendel it was commonly believed that an organism’s traits were passed on to its offspring in a blend of characteristics contributed by each parent. Mendel’s law stated that genetic material (the concept of gene was not formed yet) was inherited as distinct units, one from each parent. Due to this revolutionary discovery, Mendel was named as the “Father of Genetics”. A decade later, Morgan spotted a white-eyed male fruitfly which led him to the finding of sex linkage. Morgan became the first person to link the inheritance of a specific train (white eye) to a particular chromosome (X) [15,16]. These early works marked the dawn of our understanding of the fundamental nature of inheritance. But the road ahead was never straightforward.

People nowadays take it for granted that DNA is the genetic material passed on from one’s parents and determining ones characteristics. Actually for many decades scientists believed that proteins, instead of DNA, were the molecules that carry genetic information. Despite a lack of clear experimental proof, the main reason that hindered the scientific progress was in fact people’s intuitive bias. As DNA contains only 4 different nucleotides (A, C, T and G), while protein has 20 various amino acids to harness, no wonder people were inclined to believe that protein is more qualified to play such a vital role as storing the vast amount of genetic information. It was not until the 1940s that Avery and his colleagues found convincing experimental proof showing DNA being the chosen one [17]. In retrospect, we learn that the number of basic components matters less than the ways of their combinations.

In the early 1950s, scientists working on DNA started to use “gene”, which is essentially a fragment of DNA, to denote the smallest unit of genetic information. However, no one knew what genes look like physically, or how is DNA duplicated during the organism reproduction [18]. Then came Watson and Crick. Based on the X-ray crystallography obtained by Rosalind Franklin, they depicted the double-helix structure model for DNA, which turned out to be astonishingly accurate [3]. The single-page paper titled “A Structure for Deoxyribose Nucleic Acid” not only illustrated beautifully what DNA looks like, but also answered the questions on how DNA replication could be carried out. The discovery of the double helix structure of DNA represents one of the most remarkable scientific achievements of human being, and it gave rise to modern molecular biology [18]. Figure 1 shows a schematic drawing of the DNA double helix structure.

Several years later, Nirenberg, Crick and collaborators deciphered the genetic code. They first figured out that each amino acid is encoded as a triplet (named codon) in terms of DNA bases. Then and by 1966, the codons for all twenty amino acids had been identified. It thus became clear how genetic information flows from DNA to messenger RNA, and to protein [19,20].

The invention of DNA sequencing method by Sanger in 1977 opened a key chapter of genomics [21]. Since then, the sequencing technology advanced rapidly [22]. In addition, with the thriving of bio-informatics, large databases and genome browsers were developed [23,25]. Together, they led to the completion of full genome sequencing of the model organism *Drosophila melanogaster*.
(the same species as Morgan’s white-eyed fly) in 2000 [26]. A year later, the first draft of the human genome sequence was released [4]. In the following years, many other whole genome sequences were published with the aid of next-generation sequencing technology [25].

2.2 Current status of genomics

Rather than putting an end to genomics, the sequencing of more and more whole genomes not only revolutionized existent disciplines, but also opened up exciting new areas. Personalized medicine is one salient example [27]. Without individual sequence profiles of their patients, doctors previously could only diagnose a disease after the patients had already developed it. Nowadays, a doctor is able to predict whether a person is at risk of developing certain diseases based on their unique genomic constitution. As a result, the chances of preventing such disease from actually happening are greatly increased [28–30].

Moreover, genome editing (also called gene editing) is a technique that has drawn a great deal of attention in the recent years [31]. The tools in this field have expanded rapidly from zinc finger nucleases (ZFNs), transcription activation-like effector nucleases (TALENs), to clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated (Cas). These new methods enabled highly efficient, precise and cost-effective study on human and animal models of diseases [32].

Another field worth mentioning is synthetic biology. It aims to redesign and synthesize artificial organisms [33]. Driven also by technical advances, the current ambitious project – to design and synthesis of a complete yeast genome, is making incredible progress [34].

Besides DNA sequencing, RNA sequencing (RNA-seq) which directly reflects how genes are expressed in the cells, is also an important branch of genomics. The next generation sequencing technology has given a strong impetus for high throughput RNA-seq as well [35]. Especially, single cell RNA-seq has revolutionized RNA-seq by providing unprecedented resolution, and it is growing prosperously in the recent years [36,37].

The tremendous amount of data generated by those sequencing works urged
strong support from bioinformatics and computational biology. Large databases such as GenBank (the NIH genetic sequence database), Refseq (NCBI reference sequence database) and genome browsers such as Ensembl, UCSC Genome Browser, are established and continuously being improved. An expanding list of major bioinformatics institutions are setting up worldwide, National Center for Biotechnology Information (NCBI), European Bioinformatics Institute (EMBL-EBI), Wellcome Trust Sanger Institute (WTSI), Broad Institute, to name a few of them. Currently about 25 journals, 13 conferences, 8 workshops are dedicated exclusively to bioinformatics and more than 22k articles being published on the trends. Furthermore, all sorts of computational tools including deep learning are utilized for genomics.

Above all, the most exciting ongoing research in genomics is perhaps the “3D genome”. People have long been realizing that although the DNA strands appear linear, the real chromosomes in a nucleus actually form complex and dynamic three-dimensional configurations, and that plays critical roles in gene regulations and functioning. In particular, high-resolution studies of chromosome conformation has revealed that the 3D genome is hierarchically organized into large compartments composed of smaller domains called topologically associating domains (TADs). The molecular details on how these domains are formed and how they affecting genome functions are the hot topics under intensive investigations.

2.3 The next big question of genomics

Apparently the study of 3D genome is far from being completed at this moment. On the other side, based on the current speed of science, it won’t be too long before we see a relatively clear picture of the mechanisms of 3D genome dynamics. By then we will have the chances to tackle the next big question in genomics – the organization principles of the genome, both structurally and functionally. That means we will have a deep and thorough understanding of the genomes, to the point that it will guide our genome editing, genome synthesis and disease prediction with precision. If we dare look into farther future, we might be able to create artificial organisms, and we will be able to cure any human diseases through genome editing.

But, in order to reach that level of understanding, we need to combine our insights of the 3D genome with all the DNA/RNA sequencing information as well as the functional and relational genomics knowledge that we have accumulated and will do. Here we propose that applied category theory is the right language and tool to implement the combination, and we will explain the reason in the following section.

3 What is applied category theory and why is it useful for genomics

Category theory originates from pure mathematics and is known to be highly abstract. As if residing in a lofty attic, category theory appears strange even to many professional mathematicians. While unexpectedly, this once esoteric course has found itself being pretty useful in several areas outside mathematics
along with its own development in the recent years. Actually, the field of applied category theory is expanding its territory at an accelerated pace, covering quantum physics, programming language, databases and informatics, natural language processing and others [11]. Furthermore, given the fact that category theory has already been applied in many sub-fields of biology, it is surprising that an explicit connection between applied category theory and genomics is still missing today. We intend to set up such a connection, and will lay out our rationality in more details subsequently.

3.1 Category theory and its application in general

Category theory is a relatively new branch of mathematics invented by Eilenberg and Mac Lane in 1945 [8]. They were studying the unification of different mathematical fields such as geometry and algebra, and they managed to devise a set of abstract concepts to capture the similarities between those two fields at a fundamental level [10]. Soon their work was found to be applicable to many other fields of mathematics. The basic idea of category theory is to formalize a given study within mathematics as a category, and it can be connected with other categories from different fields, as long as their structures could be aligned in a “functorial” way. In a nutshell, a category has objects (representing things) and morphisms (representing the ways to go between things) as its basic components. And two consecutive morphisms could be composed together. Besides, there is functor which maps a category to another category, and there is natural morphism going between two such functors. These ideas and the whole assembly of theories built upon them are so powerful that category theory was nominated as an alternative foundation to mathematics (replacing set theory) [10,55].

Not long after, category theorist realized that the practical value of those theories could go well beyond mathematics. In fact, category theory has been successfully applied in physics, computer science and linguistics [10]. Take quantum physics for example, a basic physical system and the measurement performed on it could be naturally modelled as a category. Concretely, different types of physical systems, be them qubits, electrons or classical measurement data, are the objects of the category. The operations are the morphisms, and consecutive applications of two operations correspond to the composition of two morphisms, and so on. Once transformed into categorical models, the physical systems could be studied formally, taking advantage of the rich repertoire of constructions and theorems in category theory. Besides, string diagram in category theory provides a unique way to visualize complex quantum computations in a much more intuitive way than traditional equations do [56, 57]. But most amazingly, category theory allows us to zoom out and see an even bigger picture. In this picture, there appear extensive analogies between physics, topology, logic and computer science, and these analogies could be precisely described using the concept of a “closed symmetric monoidal category” [58].

Further along the way, an application of category theory to science in general was introduced by David Spivak in his book “Category Theory for the Sciences” [59]. In this nice book, a tool called ologs (ontology logs), based on category theory, is invented to give structures to ideas and concepts, so that they could be expressed strictly and explicitly, and be communicated efficiently. Also, ologs encompass a database schema. In short, ologs represent a framework where scientists are able to formalize their ideas and record data about their
experiments, all in a mathematically sound way [59]. It appears that the growing breadth and depth of applications of category theory demand a field of its own. Actually, the first international conference of applied category theory in 2018 [60], along with a dedicated open access journal “Compositionality” [61], has already given birth to this new field – applied category theory (ACT). Since then, it has been attracting increasing attentions, its community has been expanding rapidly, and it has been reaching out wider territories. A more inclusive but not exhaustive list of ongoing applications outside mathematics would have in it quantum computing, natural language processing, programming languages, network theory, databases and information theory, logic and proof theory, resource theory, process theory, game theory, statistics and probability theory, biology (detailed right after) and cybernetics [11,60,62–64].

3.2 Category theory applied in biology

The theoretical biologist Robert Rosen was among the first to use category theory in system biology. He asked the most fundamental questions such as “What is life?” And he argued that a reductionistic approach was inadequate for the studying of the functional organization of living organisms [65,66]. Instead, Rosen proposed an alternate paradigm in which he modelled an organism as a “complex system” that cannot be fully understood by reducing to its parts. Under this frame, complexity refers to the causal impact of organization on the system as a whole, and relationships among organized matter rather than particular matter alone were put into focus. The model known as (M,R) systems, and the discipline named “Relational biology”, adopted a category theoretic method [67–70].

On the other hand, different from modelling the whole organism as what Rosen did, there exist several important studies working on the molecular level. An early example is Carbone and Gromov’s “Mathematical slices of Molecular Biology”, in which they modelled the spatial structure of DNA, RNA and protein by using topological surfaces and spaces [71]. Later on, Sawamura et al. made an effort to systematize molecular and genetic biology using category theory. In their work, the authors constructed a wallpaper pattern to describe the algebraic features of DNA base sequences [72]. More recently, Remy Tuyeras built a much stronger connection between genetics and category theory through a series of papers. There he defined a class of theories and related models, and recovered various aspects of genetics categorically. Under his framework, DNA sequencing and alignment, homologous recombination, haplotypes, CRISPR editing and genetic linkage could all be formalized using mathematical language, and the mechanisms of genetics could be illustrated clearly [73–75].

In addition, a category theoretic way to study neuroscience has been practiced from time to time. Most prominently, the book “Memory Evolutive System; Hierarchy, Emergence, Cognition”, authored by Ehresmann and Vanbremeersch, provides a comprehensive mathematical model for autonomous evolutionary systems in neuroscience. The main idea of this book is to use the notion of colimit from category theory to describe how complex hierarchical systems are organised [76,77]. Besides, it also lays out the potentials for higher dimensional algebra and higher categories to model the structure of the brain, as was proposed in an earlier work [78].
Beyond neuroscience and perhaps even beyond biology, category theory has been adopted to demystify consciousness as well. We exemplify two pieces of the latest work here, both of which take advantage of the graphical language of process theory. Process theory is an abstract framework describing how processes can be composed, and it is essentially symmetric monoidal categories. One study of the two gets its inspiration from the Yogacara school and characterises the key feature of consciousness as “other-dependent nature”, i.e., the nature of existence arises from causes and conditions. The other work is based on Integrated Information Theory (IIT) developed by Tononi and collaborators, which proposes that consciousness originates from integrated internal dynamics in the brain.

3.3 Features of genomics data match the strength of applied category theory

So far, category theory has not been explicitly applied to genomics, while apparently it should be. The reason is that applied category theory has all the advantages to address the needs from genomics study, whose data have the main features explained next.

First of all, genomics data is highly diversified and heterogeneous. There are about 8.7 million different species on the planet, each with a unique genome of its own. As genomics concerns the genomes of all sorts of organisms, the diversity of genomics data comes naturally from the multiplicity of species. On the other side, the heterogeneity of high-throughput biotechnologies have created miscellaneous data types from various perspectives, e.g., Chromatin accessibility, DNA methylation, and mRNA/microRNA expression.

Second, the genomics data has the hierarchical and multi-scaled features. In practice, the genome itself is organized in hierarchical manner. Concretely, the spatial organization of chromatin in the nucleus has important impact on the regulation of gene expressions. Experiments that map high-frequency contacts between chromatin segments have revealed the existence of topological associating domains (TAD), which incorporate most of the regulatory interactions. Especially, TADs are found to be not homogeneous structural units, but organized into hierarchies, i.e., large TADs often contain subTADs nested inside them.

Third, genomics information contains intricately interconnected relationships. As mentioned above, inside the nucleus, chromatin forms complex and motional 3D shapes, and therefore the local chromatin segments contact each other in a coordinated yet dynamic way. Also, the transcription factors controls the expression of their target genes which together constitute sophisticated gene regulatory networks. In addition, outside the nucleus while inside a cell, the proteins interact with each other forming signalling pathways and cross-talks among those pathways.

Together, these characteristics of genomics data pose a formidable challenge for any attempts to integrate them. Luckily and reassuringly, applied category theory offers promising solutions due to the following reasons. (1) The abstractness of category theory allows for an opportunity to extract the general features or common underlying structures (which are not obvious on the surface) from the diverse data, and to present them in a unified framework. (2) Compositionality, the essence of category theory, together with scalability (to higher
categories) make applied category theory an ideal tool to model large-scale, multi-layer systems. (3) An extremely rich and ingenious set of gadgets such as functor, natural transformation, adjoint, limit and so on, provides powerful language to describe all sorts of relationships between objects, as well as the relationships between relationships.

4 Connecting the two fields – a practice

Due to what has been explained in the previous sections, a practice to really connecting genomics with category theory is worth of time and efforts. In other words, we’ve answered the question of why, and we need to solve the problem of how. To do so, there are two main routes to take: one is to make use of the currently available models or theories, and the other is to build a categorical framework for genomics from scratch. In this work we will first review some initial attempts from the former, and then give a preliminary draft for the latter.

4.1 language, network and ontology – three bridges

Figure 2 illustrates a summary of three topics serving as bridges or tunnels that connect the two fields. We will give a brief description for each of them in this section. The readers are suggested to look into the individual manuscripts for further details.

Figure 2: Three bridges connecting applied category theory with genomics

One bridge is the language perspective. As in its physical form, the genome is long strings of DNA sequences consisting of A, C, T and G, it is natural to think of the genome as a text written in a language with the alphabet of those four letters (nucleotides). Consequently, the tools and theories that have been developed for natural language processing could be borrowed for the study
of genomes. In practice, this enterprise has been taken on for several decades [92-99].

On the other side, category theory has been used for natural language processing for almost a decade as well. Especially, a mathematical model called DisCoCat (Categorical Compositional Distributional Model) was created to compute the meaning of a sentence from the meanings of its constitutive words. Concretely, the DisCoCat model unifies the distributional representations of word meanings in vector spaces with the compositional grammar types of words in a pregroup, and it takes advantage of the pregroup algebra to transform the meanings of individual words into a meaning of the whole sentence. The key idea behind DisCoCat model is that both vector spaces and pregroup share the same high level mathematical structure – a compact closed monoidal category [100].

As a trial to harness the DisCoCat model for the genome language, a protein linguistics was considered [101]. Proteins are the products of genes that actually carry out the biological functions. Each protein is in turn composed of one or more distinguish domains, which are the functional units of the protein. Interestingly, the domains seem to assemble into proteins in a modular and grammatical fashion [102,103]. This feature of protein enables us to take a language analogy, where a protein could be viewed as a sentence and its domains as words, and biological functions correspond to meanings. Similar to natural language where words are stable while their combinations into sentences are diversified, the domains are evolutionarily conserved while their combinations into proteins are quite flexible. Therefore, although we now know the function of most domains, our ability to predict functions of novel proteins are limited [104,105]. Since DisCoCat model could calculate the meaning of a sentence from words, it provides a novel way to predict the function of a protein from its domains [101]. Figure 3 shows a transferring of the basic schema of DisCoCat model to the analogous protein linguistics.

The other bridge concerns the network connections. In genomics, gene regulatory network (GRN) is the most common description of the intrinsic interactions between genes that govern their expression levels. Several computational approaches have been used to model GRN including boolean network, Bayesian
network, differential equations model, Petri nets, etc. In particular, Petri nets, with a strong theoretical support and a broad application community, excel in modelling concurrent dynamic systems in general. A Petri net, by definition, is a bipartite directed graph containing places and transitions connected by directed arcs. A place can hold resources called tokens, and the flow of tokens from one place to another through the transition between them captures the process of state updates of a dynamic system. Furnished with rules for those updating, Petri nets are able to specify clearly the structure and behavior of certain processes. Therefore, although they haven’t been extensively explored for GRN, Petri nets provide a very promising tool to advance GRN study in the future.

However, standard Petri nets are not composable, which limits their application in modelling large scale networks. This issue has been solved when Petri nets were put into the framework of category theory, and when the concept of “open Petri nets” were established. The basic idea of an open Petri net involves designating certain places in a Petri net as input or output, and through them tokens are allowed to flow in or out of the Petri net, and thus the net is made open. The input and output sets are objects and the open Petri net is the morphism between them, and they form a symmetric monoidal category with both sequential and parallel composition available. If open Petri nets could be used for GRN, it would help to model large or multiscale GRNs. A rudimentary step is taken towards that direction, while more in-depth work is expected.

Another bridge takes the ontology viewpoint. In order to enable a knowledge transfer among different species, the concept of Gene Ontology (Go) was created to produce a controlled vocabulary for the annotation of gene functions. Since its birth, GO has grown into the most important tool to unify biology. As of Aug 2020, the Gene Ontology database has collected 44,262 GO terms and 8,047,076 annotations, covering 1,556,208 gene products from 4,643 species.

Currently GO is represented in the Web Ontology Language (OWL), which is a semantic web standard established by the World Wide Web Consortium (W3C). Although OWL is expressive, flexible and efficient, it is relatively insufficient in representing knowledge that is not binary, and its scalability is limited. As the GO database hosts a huge amount of information, also as the GO terms have intricate connections, a more powerful ontology language is needed.

Fortunately, as mentioned above, ontology log (olog), an ontology language based on category theory, has been devised. Basically, each olog is a category in which objects and morphisms are called types and aspects. A type in an olog represents an abstract concept such as “a gene”, and an aspect from type X to type Y denotes a way of viewing X as Y. The aspects are functional relationships so that they can be composed. Built on these simple blocks, a rich set of structures and relationships could be expressed rigidly, making olog an ideal tool for knowledge representation. The merits of ologs justify an effort to try them for gene ontology, as was practised already.

At this preliminary stage, all three topics are only touched superficially but there are outlets to go deeper. For example, in the DisCoCat for protein project,
a pregroup grammar description for protein domains is still lacking, and it can be filled by systematically analyzing the domain combinations of proteins. Also, string diagram could be introduced to formalize and visualize the calculation. In addition, once we know how to calculate the function of a protein (equivalent to the meaning of a sentence), we could then lift from DisCoCat to DisCoCirc, that is, from sentence to text \[122\]. In the language of life, that corresponds to go from gene to genome, which is exactly what we want to achieve from the beginning.

However, the point really is that the genome could be modelled or viewed in three such different lens, while applied category theory is able to provide all those various frameworks. Besides, this is just part of the story, there are much more intersections between genomics and applied category theory that are yet to be discovered. The opportunities for categorical genomics is abundant.

### 4.2 The category of genes

In this section, we will build a category for genomics from scratch. First, we review the definition of a category \[123,124\]. A category consists of the following data:

- a collection of objects: \(X, Y, Z, \ldots\)
- a collection of morphisms: \(f, g, h, \ldots\)
- for each morphism \(f\), there are specified objects called domain and codomain of \(f\); the notation \(f : X \to Y\) indicates that \(X\) is the domain of \(f\) and \(Y\) is the codomain.
- given morphisms \(f : X \to Y\) and \(g : Y \to Z\), that is, the domain of \(g\) is the same as the codomain of \(f\), there is a morphism \(g \circ f : X \to Z\) called the composite of \(f\) and \(g\).
- for each object \(X\), there is a given morphism \(1_X : X \to X\) called the identity morphism of \(X\).

These data are required to satisfy the following laws:

- Associativity: \(h \circ (g \circ f) = (h \circ g) \circ f\) for all \(f : X \to Y, \ g : Y \to Z, \ h : Z \to W\).
- Unit: \(f \circ 1_X = f = 1_Y \circ f\) for all \(f : X \to Y\).
According to this definition, the most straightforward categorical construction in genomics seems to be a category of genes, where the objects are genes and the morphisms are relationships between them. However, the actual definition of such morphisms could be tricky because the relationships between genes are intrinsically complex. As a start point, we define a pre-order relationship between genes based on their positions on the chromosome. Concretely, for a certain genome, we first order all its constituent chromosomes according to their normal nomenclature, and then for all the genes on a certain chromosome, we order them according to their start positions if the genes are on the sense strand, while to their end positions if they are on the anti-sense strand. If two genes have the same start positions, the one that finishes earlier (the shorter one) will be ordered ahead of the other one. If gene A is ordered before gene B, we will write \( A \leq B \) to denote it. The order of chromosomes is marked similarly.

To illustrate the ordering scheme, we take the fruitfly genome as an example. Figure 5 depicts the components of a fly genome.

![Figure 5: Drosophila melanogaster chromosomes (diagram created by Steven J. Baskauf)](image)

We can see that fruitflies have 5 distinctive chromosomes, and they could be ordered as \( \text{Chr.X} \leq \text{Chr.Y} \leq \text{Chr.2} \leq \text{Chr.3} \leq \text{Chr.4} \). According to our rules, all the genes on \( \text{Chr.X} \) are ordered before those on \( \text{Chr.Y} \), which in turn are placed before those on \( \text{Chr.2} \), and so on. Figure 6 shows the ordering of some hypothetical genes on \( \text{Chr.X} \) and \( \text{Chr.2} \). In this example, gene A ranks the “lowest” as it is on chromosome X. Gene B and gene C start at the same point while gene C finishes earlier, so gene C sits before gene B in the order list. As for gene E, the start point of gene E locates after that of gene D, however, gene E is on the anti-sense strand, and therefore it ranks before gene D.

Finally, we give a sketch of the construction of a category of genes based on the pre-order relation explained above. It is expected that more variants of categories of genes will be devised in the future.

The category of genes \( G \) for a specific species consists of the following com-
ponent:
• All the genes of that species as objects.
• The pre-order relation between genes as morphism, denoted as \( \leq \). And
the pre-order is defined with the rules:
  1. the chromosomes are ordered according to normal convention
  2. if chromosome I is ordered before chromosome II, then all genes on I
     are ordered before II
  3. on the same chromosome, genes are ordered according to their start
     positions
  4. if a gene is on the anti-sense strand, the stop position is taken for
     ordering instead of the start position
  5. if two genes start on the same position, the shorter gene is ordered
     before the longer one.
• Each gene A is related to itself (\( A \leq A \)), denoted as \( id_A \), this is the identity
  morphism on objects.
• If three genes A, B, and C have the relations \( A \leq B \), and \( B \leq C \), then
  there is relation \( A \leq C \), and this is composition on morphisms.

The associativity and unit laws fit naturally with the pre-order relation on \( G \). Interestingly, there is an important “dual” notion in category theory, where
we get a dual/opposite category with the same objects as the original one but
all morphisms reversed \([123][124]\). The dual category for \( G \) would be named \( G^{op} \),
and it takes care of the anti-sense strand in reality.

5 Conclusion and future work

Applying category theory to genomics is an exciting new field to explore. We
previously made some efforts in three different perspectives. However, it seems
necessary to explicitly propose categorical genomics as a field of its own, so that
those individual puzzles could be incorporated into a big picture, and holes be
revealed for future adventures. More importantly, with a dedicated name and
its significance explained, we anticipate this new field could draw attentions
from both category theorists and genomicists, and allow them to work together
to uncover the unknown organizational principles of the genome – the marvel
of life (itself being the marvel of earth).

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