CATEGORY THEORY FOR GENETICS II:
GENOTYPE, PHENOTYPE AND HAPLOTYPE

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Abstract. In this paper, we use the language of pedigrad, introduced in previous work, to formalize the relationship between genotypes, phenotypes and haplotypes. We show how this formalism can help us localize the variations in the genotype that cause a given phenotype. We then use the concept of haplotype to formalize the process of predicting a certain phenotype for a given set of genotypes.

1. Introduction

1.1. Short presentation. The goal of the present article is to make a first step toward the categorical modeling of a multi-level complex systems by linking the concepts of genotype, phenotype and haplotype. While this is only a first step, the article shows how this basic formalization can already be used to reason about the detection of genetic variations that are responsible for certain phenotypes and the prediction of these phenotypes for a given sample of individuals.

1.2. Motivations. Epidemiology has seen, these last 30 years, a growing interest in Mendelian randomization, a method of patient randomization that allows the identification of the causes of certain diseases more robustly than other classical sampling methods that would not focus on genotypes [21, 1, 19]. Mendelian randomization takes advantage of biological randomization processes, such as Mendelian segregation and homologous recombination, to better determine the causes of a given set of phenotypes [1].

There has been an increasing amount of articles about how to design experiments that would best use this randomization method [15, 3, 1], but a sound theoretical framework allowing phenotypic inference is still very much needed as the model of Mendelian randomization comes with many subtleties [15, 3, 20]. The goal of the present article is to make a first step toward the development of such a theoretical framework by clarifying the relationship between genotypes, phenotypes and haplotypes, which are three of the main components used in Mendelian Randomization [19]. Note that frameworks that would formalize the application of Mendelian randomization is mostly motivated by the design of successful drug development processes for the pharmaceutical industry [21, 1, 3].

The present paper is also the first step toward a greater goal, namely that of unifying the various levels of biology within a same language. Such a framework would allow the clarification of new or future concepts, whose complexity can tend to increase due to the incoming of large amount of data and would thus facilitate the dissemination of knowledge between researchers. Such a unification has been shown to be important [23] for the reason that “increasingly sophisticated modeling concepts remain to be developed before the promise of systems biology can be fully realized” (see [23, section 4]). In this paper, our goal is to link three different levels of biology, namely an internal level (the genotypes), an external level (the phenotypes) and an interaction level (the haplotypes) and to use the developed formalism as a guideline in the study of these levels.

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1.3. **Road map and results.** In this paper, we aim to formalize the relationship between the concepts of genotype, phenotype and haplotype by using categorical structures. These structures are then used to reason about the prediction of phenotypes for a given sample.

Since the present work builds on previous work (see [22]), we start by recalling the basic definitions of our formalism in section 2 – the main notions being that of pedigrad and that of chromology. As was the case in [22], section 2 includes the presentation of a problem that is used throughout the paper to illustrate the various definitions introduced herein (see section 2.1).

In section 3.1, we recall some of the main constructions of [22], which were originally introduced to study sequence alignments. In our case, we will use these structures to model the chromosomal structure of the genome, which involves the consideration of pairs of alleles for each gene.

The main part of the paper is contained in section 4 whose goal is to show that pedigrads can be used to model the concept of haplotype (see Corollary 4.56, which is deduced from Theorem 4.55 and Theorem 4.54). Specifically, pedigrads are used to formalize the link between phenotypes and haplotypes in terms of an epimorphism of the following form (see section 4.7, section 4.9 and section 5.1).

\[ f : \text{Phenotypes} \rightarrow \text{Haplotypes} \]

Section 4 first starts by recalling the definition of idempotent commutative monoids and some of its associated properties, from section 4.1 to section 4.3, and use these to formalize the link between genotypes and phenotypes as a span of functors in the category of idempotent commutative monoids (see section 4.4). In Example 4.19, we show how the concepts of coequalizer (section 4.6), monomorphism and epimorphism (section 4.5) can help us reason about this span structure. Then, from section 4.7 to section 4.10, we use these concepts to formalize the process of predicting phenotypes from a limited knowledge in terms of the previously mentioned epimorphism. The limited knowledge attached to this construction implies that the codomain of the epimorphism has to be of the certain form. We achieve this construction through the concept of pedigrad (see the discussion at the end of section 4.7 and Remark 4.44).

Finally, in section 5, we see how the fibers of this epimorphism can be used to predict the phenotypes of a given population of a certain haplotype.

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2. **Chromologies and Pedigrads**

2.1. **Main example.** As was done in [22], we will make use of a main example to motivate the different concepts introduced herein. Most of our examples will aim to demonstrate how the different definitions and results of the present paper help understand the main example.

Thus, without any further introduction, our problem will look at pairs of alleles at a particular locus in the genome of three different individuals whose phenotypes are known (e.g. healthy, diseased, etc.). Our goal will be to identify the parts of the genome that are responsible for each of the observed phenotypes and to use this information to make some type of prediction.

In theory, the most efficient way to establish a mapping between the genotypes and the phenotypes would be to look at the progeny that can be produced from the three individuals to see if the recombination of their genes can lead to identifying some sort of pattern by using a pigeonhole-principle-like reasoning. Of course, this method is absolutely not practical, and one usually need to instead look at the genotypes of individuals belonging to the same haplogroups as those of our individuals. Another alternative would be to look at the genotype of the family members of our individuals.
In our case, we will consider the following set of individuals whose genetic data, for the same type of chromosome at the same locus, is given by the following pair of alleles.

| Individuals | Pair of alleles                  |
|-------------|----------------------------------|
| Alice       | ACCATTAGCTACCTATAC ACCACTAGCTACATATGC |
| Brian       | AGCATTAGCTACCTATAC ACCACTAGCTACATATTC |
| Charles     | AACATTAGCTACCTATAC ACCACTAGCTACATATTC |

In genomics, one usually analyzes large amounts of DNA-sequence data to find the variations that are responsible for a given phenotype. Of course, identifying these variations is not easy as many processes may play a role in creating the noticeable differences (food, environment, etc.). In general, these variations are located at a single position within a DNA segment. These variations are called single nucleotide polymorphism (SNP) when they can be find within at least two non-negligible percentages of the population (see [8]).

SNP are usually used to classify populations in terms of haplogroups – the common genetic information shared by a group of individuals is called the haplotype (see [8, 9, 2]).

The fact that certain haplogroups are more susceptible than others to certain diseases is linked to the fact that certain SNPs are in linkage disequilibrium [8] with the disease, meaning that there is a non-trivial genetic linkage [8] between the mutations causing the disease and those SNPs. Here, it is important to understand that the SNPs themself are not necessarily responsible for the disease, but are often appearing on the same segment because homologous recombination tend to keep them together [13, 25, 18, 5]. In this case, the SNPs are referred to as markers for the disease.

Sickle-cell anaemia (SCA) is a very famous example of disease that is caused by a single-nucleotide variation in the DNA [6]. The disease is known to be associated with beta S-globin haplotypes [10]. On the other hand, certain diseases, such as retinis pigmentosa [24], can be associated with a large number of mutations, which may not all need to exist to trigger the disease. In the case of retinis pigmentosa, the configurations leading to the disease are still not understood (see [24]). This disease is known to be prevalent in Asian and Caucasian populations.

For our problem, we will suppose that our three individuals are associated with a certain phenotype, namely either diseased or healthy, as shown below, in the left-hand side table. In the right-hand side table, the different variations that could be responsible for these phenotypes are shown with their positions in the pair of alleles.

| Individuals | Phenotypes | Positions in the alleles |
|-------------|------------|-------------------------|
| Alice       | Diseased   | C T C A C A             |
| Brian       | Healthy    | G T G T G G             |
| Charles     | Diseased   | A T G T A T             |

Of course, as mentioned earlier, only considering this amount of data is not sufficient to determine where the markers for the disease are. Ideally, we would like to consider some data about a population that is related to Alice, Charles and Brian, such as their progeny, which is produced by homologous recombination. Recall that homologous recombination is the process of shuffling two chromatides together in a way that essentially preserves the positions of the nucleotides (see section 4.7). For instance, the recombination of the two words ab and AB could be given by one of the following four words: ab, aB, Ab and AB.
In our case, we will consider the following progeny, which is divided in several tables for different recombination combinations between the alleles of Alice, Brian and Charles (namely, Alice with Brian; Brian with Charles; Alice with Charles; and Alice with Brian and Charles over several generations).

| Indiv. | Pair of alleles | Phenotypes |
|--------|----------------|------------|
| P1     | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Healthy |
| P2     | AGCATTAGCTACATATGC AGCATTAGGTACCTATAC | Healthy |
| P3     | AGCATTAGCTACATATGC AGCATTAGGTACCTATAC | Healthy |
| P4     | AGCATTAGCTACATATGC AGCATTAGGTACCTATAC | Healthy |
| P5     | AGCATTAGCTACATATGC AGCATTAGGTACCTATAC | Healthy |
| P6     | AGCATTAGCTACATATGC AGCATTAGGTACCTATAC | Healthy |

| Indiv. | Pair of alleles | Phenotypes |
|--------|----------------|------------|
| P7     | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Diseased |
| P8     | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Diseased |
| P9     | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Healthy |
| P10    | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Diseased |
| P11    | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Diseased |
| P12    | ACCATTAGCTACATATGC ACCATTAGGTACCTATAC | Healthy |

Our goal is to use the previous data set (1) to determine what the markers that characterise the disease are, (2) to understand the dominance relationships between them and (3) to use this information to predict the phenotype of individuals that are not part of our data set. The only knowledge that we have is that the previous individuals all descend from Alice, Brian and Charles by homologous recombination of their alleles. This knowledge will later be integrated in terms of a pedigrad in the category of idempotent commutative monoids so that the associated chromology will specify where the recombination operations occur.

2.2. Pre-ordered sets.

**Definition 2.1** (Pre-ordered sets). A *pre-ordered set* consists of a set $\Omega$ and a binary relation $\leq$ on $\Omega$ satisfying the following logical implications.

1) (reflexivity) for every $x \in \Omega$, the relation $x \leq x$ holds;

2) (transitivity) for every $x, y, z \in \Omega$, if $x \leq y$ and $y \leq z$ hold, then so does $x \leq z$.

**Example 2.2.** The set $\{0, 1\}$ is a pre-ordered set if one sets $0 \leq 1$; $0 \leq 0$ and $1 \leq 1$. The resulting pre-ordered set is usually known as the Boolean pre-ordered set and the values 0 and 1 are usually denoted as *false* and *true*, respectively.

**Example 2.3.** For every positive integer $n$, the $n$-fold Cartesian product $\{0, 1\}^n$ of the pre-ordered set given in Example 2.2 is equipped with a pre-order relation $\leq$ that compares two tuples in $\{0, 1\}^n$, say of the form $(x_1, \ldots, x_n) \leq (y_1, \ldots, y_n)$, if, and only if, the relation $x_i \leq y_i$ holds for every $1 \leq i \leq n$. 
Remark 2.4 (Pre-order categories). A pre-ordered set is equivalently a category in which there exists at most one arrow between every pair of objects. In the sequel, a pre-ordered set will sometimes be called a pre-order category to emphasize its categorical nature.

Definition 2.5 (Order-preserving functions). Let \((\Omega_1, \leq_1)\) and \((\Omega_2, \leq_2)\) be two pre-ordered sets. We shall speak of an order-preserving function from \((\Omega_1, \leq_1)\) to \((\Omega_2, \leq_2)\) to refer to a function \(f : \Omega_1 \rightarrow \Omega_2\) for which every relation \(x \leq_1 y\) in \(\Omega_1\) gives rise to a relation \(f(x) \leq_2 f(y)\) in \(\Omega_2\).

Convention 2.6 (Notation). We shall denote by \(\text{pOrd}\) the category whose objects are pre-ordered sets and whose morphisms are order-preserving functions.

Example 2.7 (Projection). For every positive integer \(n\), the \(n\)-fold Cartesian product \(\{0, 1\}^n\) of Example 2.3 is equipped with a canonical collection of \(n\) functions \(\pi_i : \{0, 1\}^n \rightarrow \{0, 1\}\), for each \(i \in \{1, \ldots, n\}\), where a function \(\pi_i\) sends a tuple \((x_1, \ldots, x_n)\) in \(\{0, 1\}^n\) to its \(i\)-th component \(x_i\) in \(\{0, 1\}\). These functions obviously preserve the order relations of \(\{0, 1\}^n\) in \(\{0, 1\}\) and thus define morphisms in \(\text{pOrd}\).

2.3. Finite sets of integers. For every positive integer \(n\), we will denote by \([n]\) the finite set of integers \(\{1, 2, \ldots, n\}\). We will also let \([0]\) denote the empty set. In the sequel, for every non-negative integer \(n\), the set \([n]\) will implicitly be equipped with the order associated with the set of integers (note that the restriction of this order on \([0]\) is the empty order).

2.4. Segments. Let \((\Omega, \leq)\) denote a pre-ordered set. A segment over \(\Omega\) consists of a pair of non-negative integers \((n_1, n_0)\), an order-preserving surjection\(^1\) \(t : [n_1] \rightarrow [n_0]\) and a function \(c : [n_0] \rightarrow \Omega\).

Remark 2.8 (Representation). Recall that segments are equipped with a canonical graphical representation (see [22]). For a segment \((t, c)\) as defined above, the finite set \([n_1]\) represents the range of elements composing the segment while the fibers \(t^{-1}(1), \ldots, t^{-1}(n_0)\) of the surjection \(t : [n_1] \rightarrow [n_0]\) gather these elements into patches (see the brackets below).

\[
t = (\bullet \bullet \bullet)(\bullet \bullet \bullet)(\bullet \bullet \bullet \bullet \bullet)(\bullet \bullet \bullet \bullet \bullet)
\]

Finally, each patch of the segment is associated with ‘colors’ in \(\Omega\) that are specified by the map \(c : [n_0] \rightarrow \Omega\). For instance, taking \(\Omega\) to be the Boolean pre-ordered set \([\text{false} \leq \text{true}]\) of Example 2.2 and taking \(c\) such that \(c(1) = \text{false}\), \(c(2) = \text{true}\), \ldots, \(c(n_0 - 1) = \text{true}\), and \(c(n_0) = \text{true}\) will color all the elements of \([n_1]\) living in the fibers \(t^{-1}(1), t^{-1}(2), \ldots, t^{-1}(n_0 - 1)\), and \(t^{-1}(n_0)\) in white and then in black up to the last patch, as shown below.

\[
(t, c) = (\circ \circ \circ)(\bullet \bullet \bullet)(\bullet \bullet \bullet \bullet \bullet)(\bullet \bullet \bullet \bullet \bullet)
\]

Remark 2.9 (Notations). Note that the specification of the data \(n_1\) and \(n_0\) is redundant with the data of the function \(t\) and \(c\). Later on, a segment will often be denoted as a pair \((t, c)\) and, every so often, as an arrow \((t, c) : [n_1] \twoheadrightarrow [n_0]\).

Convention 2.10 (Domains, topologies & types). For every segment \((t, c) : [n_1] \twoheadrightarrow [n_0]\), the data \([n_1]\) will be called the domain of \((t, c)\), the data \(t\) will be called the topology of \((t, c)\) and the data \((n_1, n_0)\) will be called the type of \((t, c)\). The type of a segment will always be specified as an arrow of the form \([n_1] \twoheadrightarrow [n_0]\).

Definition 2.11 (Homologous segments). Two segments \((t, c)\) and \((t', c')\) over \(\Omega\) will be said to be homologous if their topologies \(t\) and \(t'\) are equal.

Definition 2.12 (Quasi-homologous segments). Two segments \((t, c) : [n_1] \twoheadrightarrow [n_0]\) and \((t', c') : [n'_1] \twoheadrightarrow [n'_0]\) over \(\Omega\) will be said to be quasi-homologous if their domains \([n_1]\) and \([n'_1]\) are equal.

\(^1\)i.e. an order-preserving function that is a surjection.
2.5. Morphisms of segments. Let \((\Omega, \leq)\) be a pre-ordered set and let \((t, c) : [n_1] \to [n_0]\) and \((t', c') : [n_1'] \to [n_0']\) be two segments over \(\Omega\). A morphism of segments from \((t, c)\) to \((t', c')\) consists of

1) an order-preserving injection \(f_1 : [n_1] \to [n_1']\);
2) an order-preserving function \(f_0 : [n_0] \to [n_0']\);

such that the inequality \(c' \circ f_0(i) \leq c(i)\) holds for every \(i \in [n_0]\) and the following diagram commutes.

\[
\begin{array}{ccc}
[n_1] & \overset{t}{\longrightarrow} & [n_0] \\
\downarrow{f_1} & & \downarrow{f_0} \\
[n_1'] & \overset{t'}{\longrightarrow} & [n_0']
\end{array}
\]

It is easy to check that the class of morphisms of segments over \(\Omega\) is stable under component-wise compositions and admits identities on every segment. We will denote by \(\text{Seg}(\Omega)\) the category whose objects are segments over \(\Omega\) and whose arrows are morphisms between these.

2.6. Pre-orders on homologous segments. Let \((\Omega, \leq)\) be a pre-ordered set and let \(t : [n_1] \to [n_0]\) be an order-preserving surjection. The subcategory of \(\text{Seg}(\Omega)\) whose objects are the homologous segments of topology \(t\) and whose arrows are the morphisms of segments for which the components \(f_0\) and \(f_1\) are identities will be denoted by \(\text{Seg}(\Omega : t)\) and referred to as the category of homologous segments (over \(\Omega\)) of topology \(t\).

**Proposition 2.13** (From [22]). For every order-preserving surjection \(t : [n_1] \to [n_0]\), the category \(\text{Seg}(\Omega : t)\) is a pre-order category.

2.7. Pre-orders on quasi-homologous segments. Let \((\Omega, \leq)\) be a pre-ordered set and let \(n_1\) be a non-negative integer. The subcategory of \(\text{Seg}(\Omega)\) whose objects are the quasi-homologous segments of domain \([n_1]\) and whose arrows are the morphisms of segments for which the component \(f_1\) is an identity will be denoted by \(\text{Seg}(\Omega \upharpoonright n_1)\) and called the category of quasi-homologous segments (over \(\Omega\)) of domain \(n_1\).

The phrasing of following statement is only meant to become relevant in the proof of Proposition 4.51, which is related to one of our main theorems (see Theorem 4.54).

**Lemma 2.14.** If there exists a morphism \((t, c) \to (t', c')\) in \(\text{Seg}(\Omega \upharpoonright n_1)\), then it is the only morphism of type \((t, c) \to (t', c')\) in \(\text{Seg}(\Omega)\).

**Proof.** Let \((\text{id}, f_0) : (t, c) \to (t', c')\) be the morphism of the statement in \(\text{Seg}(\Omega \upharpoonright n_1)\) and let \((g_1, g_0) : (t, c) \to (t', c')\) be another morphism in \(\text{Seg}(\Omega)\). Because \(g_1\) is an order-preserving inclusion of type \(n_1 \to [n_1]\), it must be an identity, so that the identity \(g_0 \circ t = t'\) holds. On the other hand, the identity \(f_0 \circ t = t'\) also holds, which means that \(g_0 \circ t = f_0 \circ t\). Because \(t\) is an epimorphism, the identity \(g_0 = f_0\) must hold. \(\square\)

Even though the particular statement of Lemma 2.14 is designed for later use, we could use it here to deduce that a category of quasi-homologous segments is a pre-order category.

**Proposition 2.15** (Already proved in [22]). For every non-negative integer \(n_1\), the category \(\text{Seg}(\Omega \upharpoonright n_1)\) of quasi-homologous segments is a pre-order category.

**Proof.** Since \(\text{Seg}(\Omega \upharpoonright n_1)\) is a subcategory of \(\text{Seg}(\Omega)\), Lemma 2.14 implies that there exists at most one arrow between each pair of objects in \(\text{Seg}(\Omega \upharpoonright n_1)\). \(\square\)
2.8. Cones. Recall that a cone in a category $C$ consists of an object $X$ in $C$, a small category $A$, a functor $F : A \to C$ and a natural transformation $\Delta_A(X) \Rightarrow F$ where $\Delta_A(X)$ denotes the constant functor $A \to 1 \to C$ mapping every object in $A$ to the object $X$ in $C$.

**Definition 2.16** (Wide spans). In the sequel, we shall speak of a wide span to refer to a cone $\Delta_A(X) \Rightarrow F$ defined over a finite discrete small category $A$ whose objects are ordered with respect to a total order (this will allow us to have canonical choices of construction).

**Example 2.17** (Wide spans). Giving a wide span in a category $C$ amounts to giving a finite collection of arrows $S := \{f_i : X \to F_i\}_{i \in [n]}$ in $C$. When the category $C$ has products, the implicit order of the set $[n] = \{1, \ldots, n\}$ can be used to give a specific representative for the product of the collection $\{F_i\}_{i \in [n]}$ in $C$.

2.9. Chromologies. A chromology is a pre-ordered set $(\Omega, \preceq)$ that is equipped, for every non-negative integer $n$, with a set $D[n]$ of cones in the category $\text{Seg}(\Omega | n)$. A chromology as above will later be denoted as a pair $(\Omega, D)$.

**Remark 2.18** (Future example). See section 4.8 for an example of a particular chromology.

2.10. Logical systems. We will speak of a logical system to refer to a category $C$ that is equipped with a subclass of its cones $W$ (see section 2.8).

2.11. Pedigrads. Let $(\Omega, D)$ be a chromology and $(C, W)$ be a logical system. A pedigrad in $(C, W)$ is a functor $\text{Seg}(\Omega) \to C$ sending, for every non-negative integer $n$, the cones in $D[n]$ to cones in $W$.

**Convention 2.19** ($W$-pedigrads). As was done in [22], we will often refer to a pedigrad in logical system $(C, W)$ as a $W$-pedigrad.

2.12. Morphisms of pedigrads. Recall that, for every pair of categories $C$ and $D$, the notation $[C, D]$ denotes the category whose objects are functors $C \to D$ and whose arrows are natural transformations in $D$ over $C$. Let $(\Omega, D)$ be a chromology and $(C, W)$ be a logical system. A morphism of pedigrads from a pedigrad $A : \text{Seg}(\Omega) \to C$ in $(C, W)$ for $(\Omega, D)$ to a pedigrad $B : \text{Seg}(\Omega) \to C$ in $(C, W)$ for $(\Omega, D)$ is an arrow $A \Rightarrow B$ in the category $[\text{Seg}(\Omega), C]$.

3. Environment functors

The goal of this section is to recall some of the constructions of [22]. Throughout the section, we shall let $(E, c)$ be a fixed pointed set and $(\Omega, \preceq)$ be a pre-ordered set.

3.1. Truncation functors. First, we recall the definition of the truncation operation given in [22]. This operation becomes useful when one wants to truncate a segment from a non-maximal color. In section 5.2, we will see that colors can be used to encode environmental factors – the truncation functor would then allow us to only look at a certain stratum of these.

**Definition 3.1** (Truncation). For every segment $(t, c) : [n_1] \to [n_0]$ over $\Omega$ and element $b \in \Omega$, we will denote by $\text{Tr}_b(t, c)$ the subset $\{i \in [n_1] \mid b \preceq c \circ t(i)\}$ of $[n_1]$. This is the set of all elements in $[n_1]$ whose images via $c \circ t$ is greater than or equal to $b$ in $\Omega$.

**Example 3.2** (Truncation). Let $(\Omega, \preceq)$ be the Boolean pre-ordered set $\{0 \leq 1\}$. If we consider the segment in $\text{Seg}(\Omega)$ given below, on the left, the truncation operation takes the values given on the right for $b \in \{0, 1\}$:

\[
(t, c) = (\bullet\bullet\bullet)(\circ\circ\circ)(\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\circ\circ\circ)
\]

\[
\text{Tr}_1(t, c) = \{1, 2, 3, 6, 7, 8, 9, 15, 16, 17\}
\]

\[
\text{Tr}_0(t, c) = [18]
\]
The extension of the previous operation to a functor on a category of segments requires the consideration of the category $\textbf{Set}_*$ of pointed sets and point-preserving maps. First, recall that there is an adjunction

$$
\begin{array}{c}
\textbf{Set} \\
\text{Set}_*
\end{array}
\quad \xleftarrow{\ F \ } \quad \xrightarrow{\ U \ } \quad
$$

whose right adjoint $U : \textbf{Set}_* \to \textbf{Set}$ forgets the pointed structure (i.e. $U : (X, p) \mapsto X$) and whose left adjoint $F : \textbf{Set} \to \textbf{Set}_*$ maps a set $X$ to the obvious pointed set $(X + \{\ast\}, \ast)$ and maps a function $f : X \to Y$ to the coproduct map $f + \{\ast\} : X + \{\ast\} \to Y + \{\ast\}$.

**Proposition 3.3** (From [22]). For every element $b \in \Omega$, the mapping $(t, c) \mapsto FTr_b(t, c)$ extends to a functor $\text{Seg}(\Omega) \to \textbf{Set}_{\ast}^{\text{op}}$ mapping every function $(f_1, f_0) : (t, c) \to (t', c')$ in $\text{Seg}(\Omega)$ to the following map of pointed sets.

$$
\begin{align*}
\text{Tr}_b^*(f_1, f_0) : FTr_b(t', c') &\to FTr_b(t, c) \\
j &\mapsto i & \text{if } \exists i \in \text{Tr}_b(t, c) : j = f_1(i); \\
j &\mapsto \ast & \text{otherwise}.
\end{align*}
$$

**3.2. Environment functors.** In this section, we construct a collection of functors $\text{Seg}(\Omega) \to \textbf{Set}$ for any pointed set $(E, \varepsilon)$ and parameter $b$ in $\Omega$ (see Definition 3.5) by using the truncation functor defined in section 3.1.

**Convention 3.4** (Notation). As in [22], the hom-set of a category $C$ from an object $X$ to an object $Y$ will be denoted as $C(X, Y)$. For instance, the set of functions from a set $X$ to a set $Y$ will be denoted by $\textbf{Set}(X, Y)$. Recall that, for any category $C$, the hom-sets give rise to a functor $C_{(-, -)} : C^\text{op} \times C \to \textbf{Set}$ called the hom-functor [11, page 27].

**Definition 3.5** (Environment functors). For every element $b \in \Omega$, we will denote by $E_b^*$ the functor $\text{Seg}(\Omega) \to \textbf{Set}$ defined as the composition of the following pair of functors.

$$
\begin{array}{c}
\text{Seg}(\Omega) \\
\text{Tr}_b^* \\
\text{Set}_{\ast}^{\text{op}} \\
\text{Set}_*(\ast(E, \varepsilon)) \\
\text{Set}
\end{array}
\quad \xrightarrow{\ } \quad
$$

**Example 3.6** (Objects). Suppose that $(\Omega, \leq)$ denotes the Boolean pre-ordered set $\{0 \leq 1\}$ and let $(E, \varepsilon)$ be the pointed set $\{A, C, G, T, \varepsilon\}$. If we consider the segment

$$(t, c) = (\bullet\bullet\bullet)(\circ\circ)(\bullet\bullet\bullet\bullet\bullet)(\circ\circ\circ)(\circ)$$

then the set $E_{b}^*(t, c)$ (where $b = 1$) will contain the following words (which have been parenthesized for clarity), among many others.

$$(AG\varepsilon)(TCAA)(TAGG\varepsilon);$$

$$(GT\varepsilon)(\varepsilon\varepsilon\varepsilon)(AGTAC);$$

$$(TAA)(GATC)(AGTTT);$$

etc.

**Example 3.7** (Morphisms). Suppose that $\Omega$ denotes the Boolean pre-ordered set $\{0 \leq 1\}$ and let $(E, \varepsilon)$ be the pointed set $\{A, C, G, T, \varepsilon\}$. If we consider the morphism of segments given below, in which we use adequate labeling to show how the first segment is included in the second one,

$$
\begin{array}{ccccccccc}
1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11 \\
\ast\ast\ast & \begin{array}{cccc}
5 & 6 & 7 & 8 & 9 \\
\circ & \circ & \circ & \circ & \circ
\end{array} \\
\rightarrow & \begin{array}{cccc}
\ast\ast\ast\ast\ast & \begin{array}{cccc}
5 & 6 & 7 & 8 & 9 \\
\circ & \circ & \circ & \circ & \circ
\end{array}
\end{array}
\end{array}$$
then the image of the previous arrow via $E^\circ_\varepsilon$ is a function whose mappings rules look as follows.

$$
\begin{align*}
(AG\varepsilon)(TCAA)(GC) &\mapsto (AG\varepsilon\varepsilon)(TCAA)(\varepsilon); \\
(GT\varepsilon)(\varepsilon\varepsilon\varepsilon)(TA) &\mapsto (GT\varepsilon\varepsilon)(\varepsilon\varepsilon\varepsilon)(\varepsilon); \\
(TAA)(GATC)(AA) &\mapsto (TAA\varepsilon\varepsilon)(GATC)(\varepsilon);
\end{align*}
$$

etc.

3.3. **Sequence alignments.** In this section, we use a particular case of a more general definition given in [22]. Specifically, the construction of Convention 3.8 correspond to an example of what was called an *aligned pedigree* in [22] while the construction of Definition 3.9 correspond to an example of what was called a *sequence alignment* in [22].

**Convention 3.8** (Notation). Let $b$ be an element in $\Omega$. We denote by $2E^\circ_\varepsilon$ the functor $\text{Seg}(\Omega) \rightarrow \text{Set}$ resulting from the composition of the three functors given in (3.1), where

- the rightmost functor is the obvious Cartesian functor of $\text{Set}$;
- the middle functor is the Cartesian product of the functors $E^\circ_\varepsilon$; $\text{Seg}(\Omega) \rightarrow \text{Set}$;
- and the leftmost functor is the obvious Cartesian diagonal functor.

(3.1) \[
\text{Seg}(\Omega) \xrightarrow{(id, id)} \text{Seg}(\Omega) \times \text{Seg}(\Omega) \xrightarrow{E^\circ_\varepsilon \times E^\circ_\varepsilon} \text{Set} \]

**Definition 3.9** (Sequence alignments). Let $b$ be an element in $\Omega$. We define a *sequence alignment* over $2E^\circ_\varepsilon$ as a triple $(\iota, T, \sigma)$ where $\iota$ is an inclusion functor $\iota : B \rightarrow \text{Seg}(\Omega)$, where $T$ is a functor $B \rightarrow \text{Set}$ and $\sigma$ is a natural monomorphism $T \Rightarrow 2E^\circ_\varepsilon \circ \iota$.

**Example 3.10** (Sequence alignments). Take $(\Omega, \preceq)$ to be the Boolean pre-ordered $\{0 \leq 1\}$ and $(E, \varepsilon)$ to be the pointed set $\{A, C, G, T, \varepsilon\}$. For any given segment $\tau$ in $\text{Seg}(\Omega)$, the set $2E^\circ_\varepsilon(\tau)$ is equal to the product $E^\circ_\varepsilon(\tau) \times E^\circ_\varepsilon(\tau)$. The following table shows what the elements contained in the set $2E^\circ_\varepsilon(\tau)$ look like for different object $\tau$ and for $b$ taken to be equal to 1. Parentheses are added to the elements of $2E^\circ_\varepsilon(\tau)$ for clarity.

| $\tau$                | $2E^\circ_\varepsilon(\tau)$ |
|-----------------------|--------------------------------|
| $(\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet\bullet
Thus, we will take $T(\text{seg}_{18})$ to be the subset of $E_1(\text{seg}_{18})$ that exactly contains the pair of alleles given in section 2.1, which are recalled and named in the following table.

| $T(\text{seg}_{18})$ | $a$ | $b$ | $c$ |
|---------------------|-----|-----|-----|
|                     | ACCATTAGCTACCTATAC | AGCATTAGGTTCGTATGC | AACATTAGGTTCATATAC |
| $P_1$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_2$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_3$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_4$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_5$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_6$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_7$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_8$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_9$               | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_{10}$            | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_{11}$            | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_{12}$            | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_{13}$            | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_{14}$            | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |
| $P_{15}$            | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC | ACCATTAGCTACATATGC |

By definition, the functor $T : B \to \text{Set}$ is equipped with an natural monomorphism $\sigma : T \Rightarrow 2E^2_1$ and the resulting triple $(\iota, T, \sigma)$ defines an obvious sequence alignment.

4. Using pedigrads of idempotent commutative monoids to model haplotypes

In this section, we use the environment functors defined in section 3 to construct pedigrads in the category of idempotent commutative monoids whose role is to model the concept of haplotype.

4.1. Idempotent commutative monoids. Recall that a monoid is a set $M$ equipped with a binary operation $\star : M \times M \to M$ and a particular element $e \in M$ that satisfy the following two axioms:

1) (Associativity) for every $x, y, z \in M$, the equation $(x \star y) \star z = x \star (y \star z)$ holds;
2) (Identity) for every $x \in M$, the equations $x \star e = x = e \star x$ hold;

Below, we give the axioms defining idempotent and commutative monoids.

**Definition 4.1** (Idempotent). A monoid $(M, \star, e)$ is said to be idempotent if for every $x \in M$, the equation $x \star x = x$ holds.

**Definition 4.2** (Commutative). A monoid $(M, \star, e)$ is said to be commutative if for every $x, y \in M$, the equation $x \star y = y \star x$ holds.

**Convention 4.3** (Notation). We will follow the usual conventions of the literature and denote every commutative monoid either as $(M, +, 0)$ or as $(M, +_M, 0_M)$. The binary operation $+$ will be called the addition while the particular element 0 will be called the zero element.

**Convention 4.4** (Naming). For convenience, we will shorten the name idempotent commutative monoid to ic-monoid.

**Example 4.5** (Generator). The set consisting of two elements, say 0 and 1, has a structure of ic-monoids whose addition operation is described by the following identities.

| + | 0 | 1 |
|---|---|---|
| 0 | 0 | 1 |
| 1 | 1 | 1 |

In the sequel, this idempotent commutative monoid will be denoted as $(B_2, +, 0)$ and called the Boolean ic-monoid.
Example 4.6 (Power sets). Recall that the power set of a set \( M \) is the set of subsets of \( M \), which we will denote as \( \mathcal{P}(M) \). This set defines an ic-monoid whose addition operation is given by the union operation and whose zero element is the empty subset. For instance, if we take \( M \) to be the set of labels \{hea, dis\}, standing for the two phenotypes Diseased and Healthy of our main example (see section 2.1), then the addition operation of \( \mathcal{P}(M) \) is described by the following table.

| \( + \) | \( \emptyset \) | {hea} | {dis} | {hea, dis} |
|-------|------|------|------|---------|
| \( \emptyset \) | \( \emptyset \) | \{hea\} | \{dis\} | \{hea, dis\} |
| {hea} | {hea} | {hea} | {hea, dis} | {hea, dis} |
| {dis} | {dis} | \{hea, dis\} | \{dis\} | \{hea, dis\} |
| {hea, dis} | {hea, dis} | {hea, dis} | {hea, dis} | {hea, dis} |

4.2. Category of idempotent commutative monoids. Let \((M, \star M, e_M)\) and \((N, \star N, e_N)\) be two monoids. Recall that a morphism of monoids from \((M, \star M, e_M)\) to \((N, \star N, e_N)\) is a function \( f : M \to N \) of sets satisfying the following two axioms.

1) for every \( x, y \in M \), the equation \( f(x \star_M y) = f(x) \star_N f(y) \) holds.
2) the equation \( f(e_M) = e_N \) holds.

Definition 4.7 (Category structure). We shall denote by \( \text{Icm} \) the category whose objects are idempotent commutative monoids and whose arrows are morphisms of monoids between them.

Example 4.8 (Yoneda correspondence). Any morphism of the form \((B_2, +, 0) \to (M, +_M, 0_M)\) in \( \text{Icm} \) comes with mappings rules of the form \( 1 \mapsto x \) and \( 0 \mapsto 0_M \). Thus, giving such a morphism is equivalent to picking out an element \( x \in M \).

Example 4.9 (From genotype to phenotype). Any morphism of the form \((M, +_M, 0_M) \to \mathcal{P}(\{\text{hea, dis}\})\) in \( \text{Icm} \) partitions the monoid \( M \) into four submonoids, namely the parts of \( M \) that are mapped to the four elements 0, hea, dis and hea + dis, respectively. Later on, we will use morphisms of monoids to link genotypes to phenotypes.

Remark 4.10 (Products). The category \( \text{Icm} \) has all products. Indeed, for every set \( A \), the product of a collection \( \{M_i\}_{i \in A} \) of idempotent commutative monoids \( \{M_i, +_M, 0_M\}_{i \in A} \) is given by the product monoid \( \prod_{i \in A} M_i \) whose element are collections of elements \( (m_i)_{i \in A} \) where \( m_i \in M_i \) for every \( i \in A \). The addition operation is given by the equation \( (m_i)_{i \in A} + (m'_i)_{i \in A} = (m_i +_M m'_i)_{i \in A} \) and the zero element is given by the collection \( (0_M)_{i \in A} \). It is straightforward to check that this structure defines a product object in \( \text{Icm} \).

Example 4.11 (Addition as a morphism). Let \((M, +, 0)\) be an object in \( \text{Icm} \). The function \( \text{sum} : M \times M \to M \) that maps a pair \((x, y)\) to the element \( x + y \) in \( M \) defines a morphism in \( \text{Icm} \). Indeed, we can easily verify that the identity \( \text{sum}(0, 0) = 0 \) holds and the following equations, holding for every \((x, y) \in M \) and \((x', y') \in M \), show that \( \text{sum} \) is a morphism of monoids.

\[
\text{sum}((x, y) + (x', y')) = \text{sum}(x + x', y + y') = x + x' + y + y' = \text{sum}(x, y) + \text{sum}(x', y')
\]

Furthermore, we can show that the morphism \( \text{sum} : M \times M \to M \) is natural in \( M \). Indeed, for every morphism \( f : (M, +_M, 0_M) \to (N, +_N, 0_N) \) in \( \text{Icm} \), the equation given below, on the left, hold for every \((x, y) \in M \), which is equivalent to saying that the diagram given on the right...
commutes.

\[ f(x) + f(y) = f(x + y) \]

\[ M \times M \xrightarrow{\text{sum}} M \]

\[ f \times f \]

\[ N \times N \xrightarrow{\text{sum}} N \]

4.3. **Universal construction of ic-monoids.** There is an adjunction of the form (4.1) between sets and ic-monoids, for which the left adjoint \( F \) maps a set \( S \) to the free ic-monoid generated over \( S \) (see the discussion below) while the right adjoint \( U \) is the obvious forgetful functor.

\[
\begin{array}{c}
\text{Set} \\
\xrightarrow{\mathsf{F}} \\
\xleftarrow{\mathsf{U}} \\
\text{Icm}
\end{array}
\]

For every set \( S \), the ic-monoid \( F(S) \) correspond to the set of finite subsets of \( S \) for which the addition is given by the union operation and the zero element is given by the empty set.

**Example 4.12** (Power sets versus free ic-monoids). If we take \( S \) to be a finite set, then the image \( F(S) \) correspond to the power set of \( S \). For instance, the free idempotent commutative monoid \( F(\{\text{he, dis}\}) \) correspond to the monoid described in Example 4.6.

For every set \( S \), the unit \( \eta_S : S \to UF(S) \) of adjunction (4.1) sends every element \( x \) in \( S \) to the singleton \( \{x\} \) in \( F(S) \) while, for every ic-monoid \( (M,+),0) \), the counit \( \mu_S : FU(M,+),0) \to (M,+),0) \) of adjunction (4.1) sends the empty set to 0 and sends every non-empty finite set \( \{a_1,a_2,\ldots,a_n\} \subseteq M \) to the following finite sum in \( (M,+),0) \).

\[
\sum_{i=1}^{n} a_i = a_1 + a_2 + \cdots + a_n
\]

**Remark 4.13** (Representation). For every set \( S \), a finite subset \( \{a_1,a_2,\ldots,a_n\} \) of \( S \) can be represented by the finite sum given in (4.2) in \( F(S) \) if one identifies every singleton \( \{a_i\} \) in \( F(S) \) with the element \( a_i \) in \( S \).

4.4. **Linking genotypes to phenotypes.** The goal of this section is show how morphisms of the functor category \([\mathsf{Seg}(\Omega), \mathsf{Icm}]\) can be used to formally link genotype to phenotype. Throughout the section, we shall let \((E,\varepsilon)\) be a pointed set and let \((\Omega,\preceq)\) be a pre-ordered set.

**Convention 4.14** (Notation). From now on, for every set \( S \), we will denote by \( \Delta S \) the constant functor \( \Delta_{\mathsf{Seg}(\Omega)}(S) : \mathsf{Seg}(\Omega) \to \mathsf{Set} \) (see section 2.8).

**Definition 4.15** (Phenotypic expression). Let \( b \) be an element in \( \Omega \) and let \( (\iota,T,\sigma) \) be a sequence alignment over \( 2E_b^\varepsilon \) (see Definition 3.9). A **phenotypic expression** for \( (\iota,T,\sigma) \) is a morphism \( \varphi : T \Rightarrow UF\Delta S \circ \iota \) in \([B,\mathsf{Set}]\).

**Example 4.16** (Phenotypic expression). Take \((\Omega,\preceq)\) to be the Boolean pre-ordered \( \{0 \leq 1\} \) and \((E,\varepsilon)\) to be the pointed set \( \{A,C,G,T,\varepsilon\} \). In Example 3.10, we constructed a sequence alignment \( (\iota,T,\sigma) \) over \( 2E_1^\varepsilon \) that contained the pair of alleles of section 2.1. In this example, we show that the different phenotypes associated with the pairs of alleles of section 2.1 can be specified as a phenotypic expression for the sequence alignment \( (\iota,T,\sigma) \).

To see this, take \( S \) to be the set of labels \( \{\text{he, dis}\} \), which was already used in Example 4.6. Recall that the domain of the inclusion functor \( \iota : B \to \mathsf{Seg}(\Omega) \) consisted of a single element, called \( \mathsf{seg}_{i_8} \), whose form is recalled below.

\[
\mathsf{seg}_{i_8} = (\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)(\bullet)
\]

By definition, the image of the segment \( \mathsf{seg}_{i_8} \) via the functor \( UF\Delta S \circ \iota : B \to \mathsf{Set} \) is equal to the underlying set of the free ic-monoid \( F(S) = \mathcal{P}(\{\text{he, dis}\}) \) described in Example 4.12.
and Example 4.6. We then construct a function \( T(\text{seg}_{18}) \to \mathcal{P}(\{\text{hea}, \text{dis}\}) \) by considering the mapping rules given in the following table. These mappings respect the associations given in section 2.1.

| \( T(\text{seg}_{18}) \to \mathcal{P}(\{\text{hea}, \text{dis}\}) \) |
|-----------------|-----------------|-----------------|
| \( a \mapsto \{\text{dis}\} \) | \( b \mapsto \{\text{hea}\} \) | \( c \mapsto \{\text{dis}\} \) |
| \( p_1 \mapsto \{\text{hea}\} \) | \( p_2 \mapsto f \{\text{hea}\} \) | \( p_3 \mapsto \{\text{hea}\} \) |
| \( p_4 \mapsto \{\text{hea}\} \) | \( p_5 \mapsto \{\text{hea}\} \) | \( p_6 \mapsto \{\text{hea}\} \) |
| \( p_7 \mapsto \{\text{dis}\} \) | \( p_8 \mapsto \{\text{dis}\} \) | \( p_9 \mapsto \{\text{hea}\} \) |
| \( p_{10} \mapsto \{\text{dis}\} \) | \( p_{11} \mapsto \{\text{dis}\} \) | \( p_{12} \mapsto \{\text{hea}\} \) |
| \( p_{13} \mapsto \{\text{hea}\} \) | \( p_{14} \mapsto \{\text{hea}\} \) | \( p_{15} \mapsto \{\text{hea}\} \) |

Note that a mapping toward the element \( \{\text{hea}, \text{dis}\} \) can be used when the same genotype happen to be associated with several phenotypes. In this case, the genetic data responsible for this phenotype may have markers in a region that is not looked at.

In order to localize the DNA patches that are responsible for the phenotype \( \text{dis} \) and their degree of dominance on the other markers, we need to find the smallest set of minimal regions that always lead to a diseased state without exception. Then, the common patterns existing between the genetic data on these regions will inform us about the possible variations causing the phenotype \( \text{dis} \).

To isolate the regions of \( \text{seg}_{18} \) that are responsible for the phenotype \( \text{dis} \), we will need to extend the functor \( T \) over the whole category of segments \( \text{Seg}(\Omega) \). We will need to do so in a way that is compatible with both the natural transformation \( \sigma : T \Rightarrow 2E_\ast \circ \iota \) and the phenotypic expression \( \varphi : T \Rightarrow UF \Delta S \circ \iota \). Here, category theorists will probably recognize a need for a left Kan extension along \( \iota : B \to \text{Seg}(\Omega) \).

In [22], right Kan extensions were used to extend sequence alignments on the whole category of segments. For the present article, we will use the dual notion, namely left Kan extensions.

\textbf{Remark 4.17 (Left Kan extensions).} Let us recall that left Kan extensions in \( \text{Set} \) can be defined in terms of a colimit construction (see [11, Chap. X]). In this paper, we will only consider left Kan extensions along the inclusion functors of sequence alignments. Thus, let us consider an element \( b \) in \( \Omega \) and a sequence alignment \( (\iota, T, \sigma) \) over \( 2E_\ast \) for which \( \iota \) is of the form \( B \rightrightarrows \text{Seg}(\Omega) \).

First, we need to recall a few definitions. For every object \( \tau \) in \( \text{Seg}(\Omega) \), denote by \( (\iota \downarrow \tau) \) the category whose objects are pairs \( (\upsilon, f) \) where \( \upsilon \) is an object in \( B \) and \( f \) is a morphism \( \iota(\upsilon) \to \tau \) in \( \text{Seg}(\Omega) \) and whose arrows \( (\upsilon, f) \to (\upsilon', f') \) are given by morphisms \( g : \upsilon \to \upsilon' \) in \( B \) that make the following square commute in \( \text{Seg}(\Omega) \).

\[
\begin{array}{ccc}
\tau & \xrightarrow{f} & \tau \\
\downarrow & & \downarrow \\
\iota(\upsilon) & \xrightarrow{g} & \iota(\upsilon')
\end{array}
\]

The mapping \( (\upsilon, f) \mapsto \upsilon \) extends to an obvious functor \( \iota_\tau : (\iota \downarrow \tau) \to B \) that we can be composed with the functor \( T : B \to \text{Set} \) to form the functor \( T \circ \iota_\tau : (\iota \downarrow \tau) \to \text{Set} \). According to [11, Chap. X], the left Kan extension of \( T \) along \( \iota \) is the functor \( \text{Lan}_\iota T : \text{Seg}(\Omega) \to \text{Set} \) whose images are defined by the following colimit construction for every object \( \tau \) in \( \text{Seg}(\Omega) \).

\[(4.3) \quad \text{Lan}_\iota T(\tau) := \text{colim}_{(\iota \downarrow \tau)} T \circ \iota_\tau \]

Recall that the functor \( \iota_\tau : (\iota \downarrow \tau) \to B \) is natural in \( \tau \) over the opposite category \( \text{Seg}(\Omega)^{\text{op}} \), which means that every morphism \( h : \tau \to \tau' \) in \( \text{Seg}(\Omega) \) induces a functor \( h^* : (\iota \downarrow \tau) \to (\iota \downarrow \tau') \) for which the identity \( \iota_\tau = \iota_{\tau'} \circ h^* \) holds. In other words, the functor \( h^* \) sends an object \( (\upsilon, f) \)
in \((\tau \downarrow \iota)\) to the object \((v, h \circ f)\) in \((\tau' \downarrow \iota)\). The image of the morphism \(h : \tau \to \tau'\) via \(\text{Lan}_T\) is then the comparison morphism induced by pre-composing the diagram of the colimit with \(h^*\).

\[
\text{colim}_{(\tau \downarrow \iota)} T \circ \iota \circ h^* \xrightarrow{\text{Lan}_T(h)} \text{colim}_{(\tau' \downarrow \iota)} T \circ \iota_{\tau}
\]

It is straightforward to verify that the mapping \(\text{Lan}_T\) defines a functor \(\text{Seg}(\Omega) \to \text{Set}\).

**Remark 4.18 (From phenotype to genotype).** It is well-known (see [11, Chapter X]) that, for a given functor \(\iota : B \to \text{Seg}(\Omega)\), the operation \(\text{Lan}_\iota\) is a left adjoint for the pre-composition operation by \(\iota\) that goes from \([\text{Seg}(\Omega), \text{Set}]\) to \([B, \text{Set}]\). The counit of the adjunction at a functor \(X : \text{Seg}(\Omega) \to \text{Set}\), call it \(\nu_X : \text{Lan}_\iota(X \circ \iota) \Rightarrow X\), is then defined by the following mapping rule.

\[
\nu_X : \left(\text{colim}_{(\tau \downarrow \iota)} X \circ \iota \circ \iota_{\tau} \to X(\tau) \right)
\]

By adjointness property, any morphism \(f : A \Rightarrow B \circ \iota\) in \([B, \text{Set}]\) gives rise to a morphism \(\text{Lan}_\iota A \Rightarrow B\) in \([\text{Seg}(\Omega), \text{Set}]\) given by the composite \(\nu_B \circ \text{Lan}_\iota(f)\), which will be denoted as \(f^*\) for convenience.

In the context of this paper, we want to use the adjointness property of the left Kan extension on phenotypic expressions. Specifically, for every element \(b \in \Omega\), sequence alignment \((\iota, T, \sigma)\) over \(2E_b^\mathsf{p}\) and phenotypic expression \(\varphi : T \Rightarrow UF\Delta S \circ \iota\), the adjointness property gives us the span shown below, on the left, in \([\text{Seg}(\Omega), \text{Set}]\).

\[
\begin{align*}
\text{Lan}_T \xrightarrow{\sigma^*} 2E_b^\mathsf{p} & \xrightarrow{\varphi} \text{F} \text{Lan}_T \xrightarrow{\varphi^*} \text{F} \Delta S \\
UF\Delta S & \Rightarrow \text{F} \Delta S
\end{align*}
\]

Then, as suggested by the codomain of its vertical leg, we can use the universal property of adjunction (4.1) to send the whole span to the span given above, on the right, in \([\text{Seg}(\Omega), \text{Icm}]\).

**Example 4.19 (From genotype to phenotype).** The present example discusses the different ways in which the span of (4.4) can be used to relate genotypes to phenotypes. In this respect we will consider the same setting as the one reached at the end of Example 4.16.

First, we deduce from Remark 4.17 that the image of a segment \(\tau\) in \(\text{Seg}(\Omega)\) via the left kan extension \(\text{Lan}_T : \text{Seg}(\Omega) \to \text{Set}\) can be identified as the following set of pairs.

\[
\{(x, f) \mid x \in T(\text{seg}_{18}) \text{ and } f : \text{seg}_{18} \to \tau \in \text{Seg}(\Omega)\}
\]

The elements of the previous set can find an interpretation in the set \(2E_1^\mathsf{p}(\tau)\) through the natural transformation \(\sigma^* : \text{Lan}_T \Rightarrow 2E_1^\mathsf{p}\). More specifically, every pair \((x, f)\) in \(\text{Lan}_T(\tau)\) is interpreted via the function \(\sigma_{\tau}^* : \text{Lan}_T(\tau) \to 2E_1^\mathsf{p}(\tau)\) as the element \(2E_1^\mathsf{p}(f)(x)\), where \(x\) is considered to be taken in \(2E_1^\mathsf{p}(\text{seg}_{18})\) (by Definition 3.9).

On the other hand, because \(UF\Delta S\) is a contant functor, every pair \((x, f)\) of \(\text{Lan}_T(\text{seg}_{18})\) is sent to the phenotype associated with the pair \((x, \text{id}_{\text{seg}_{18}})\), which is, for its part, sent to the element \(\varphi_{\text{seg}_{18}}(x)\) in \(S\).

\[
2E_1^\mathsf{p}(f)(x) \longleftarrow (x, f) \longrightarrow \varphi_{\text{seg}_{18}}(x)
\]

We now give an example. Consider the following segment in \(\text{Seg}(\Omega \upharpoonright 18)\).

\[
\text{seg}_{18}' = (\circ)(\bullet)(\circ\circ)(\bullet)(\circ\circ\circ\circ\circ\circ)(\bullet)(\circ\circ\circ\circ\circ)
\]

Since there exists a unique morphism \(f : \text{seg}_{18} \to \text{seg}_{18}'\) (Lemma 2.14), the image \(\text{Lan}_T(\text{seg}_{18})\) is isomorphic to the set \(T(\text{seg}_{18})\) via the map \((x, f) \mapsto x\). Of course, from a biological point
of view, the element of $\text{Lan}_T(\text{seg}_{18})$ should not be seen as DNA sequence on $\text{seg}_{18}$ and must therefore be interpreted via the following function.

$$\sigma^*: \text{Lan}_T(\text{seg}_{18}) \to 2E_1^e(\text{seg}_{18})$$

The columns of the following table that are labeled as $\sigma^*(x, f)$ give the interpretation of every element $(x, f)$ in $\text{Lan}_T(\text{seg}_{18})$ via the function $\sigma^*$.

| $x$ | $\sigma^*(x, f)$ | $\varphi^*(x, f)$ | $\varphi^*(x, f)$ |
|-----|------------------|------------------|------------------|
| a   | CTC              | dis              | b                |
|     | CTA              |                  | GTG              |
|     |                  |                  | CCC              |
| $P_1$ | CTA              | hea              | $P_2$            |
|     | GTC              |                  | GTG              |
|     |                  |                  | CCA              |
| $P_4$ | GTC              | hea              | $P_5$            |
|     | CCA              |                  | ATG              |
|     |                  |                  | CCA              |
| $P_7$ | CTA              | dis              | $P_8$            |
|     | ATA              |                  | CCA              |
|     |                  |                  | ATT              |
| $P_{10}$ | CTA             | dis              | $P_{11}$         |
|     | CCC              |                  | ATA              |
|     |                  |                  | CTA              |
| $P_{13}$ | CCA             | hea              | $P_{14}$         |
|     | CCA              |                  | CCG              |
|     |                  |                  | GTG              |

For their part, the columns labeled as $\varphi^*(x, f)$ give the image of the element $(x, f)$ via the phenotypic expression $\varphi^*$. Interestingly, morphism (4.5) here seems to pin down the significant markers of the disease as there is no element in the columns $\sigma^*(x, f)$ that possess two different phenotypes in $\varphi^*(x, f)$ (even up to swapping of the alleles). Categorically, this perfect separation between genotypes and phenotypes can be detected by a quotient construction – let us informally describe how this can be done. First, since quotients can be more refined in $\text{Icm}$ than in $\text{Set}$, we may want to use the rightmost span of (4.4). Then, we would need to form the pullback $H$ of $F\sigma^*: F\text{Lan}_T \Rightarrow F2E_1^e$ along itself, as shown below.

$$H = \xymatrix{ & F\text{Lan}_T \\
\varpi_1 \ar[rr] & & F\sigma^* \\
\varpi_2 \ar[urr] & & \\
\text{Lan}_T \ar[u] \ar[r]_{F\sigma^*} & F2E_1^e \ar[u] }$$

The idea is then to use the pair $(\varpi_1, \varpi_2)$ to quotient the phenotypic expression by forming the coequalizer of the following pair (coequalizers will be reviewed in section 4.6).

$$H = \xymatrix{ & F\Delta S \\
\mu F\varphi^* \circ \varpi_1 \ar[rr] & & F\Delta S \\
\mu F\varphi^* \circ \varpi_2 \ar[urr] & & \\
\Delta S \ar[u] \ar[r]_{\mu F\varphi^*} & F\Delta S \ar[u] }$$

While the resulting coequalizer arrow $e: F\Delta S \Rightarrow Q$ is usually not a monomorphism (i.e. some elements are identified as the same), in our case, the perfect separation between genotype and phenotype noticed earlier would force the evaluation of the coequalizer at $\text{seg}_{18}$ (shown below) to be a monomorphism.

$$e_{\text{seg}_{18}}: F\Delta S(\text{seg}_{18}) \Rightarrow Q(\text{seg}_{18})$$

Thus, we see that we can categorically localize the markers of a certain phenotype by verifying whether certain arrows are monomorphism or not. The idea would then be to find the segment that possesses the fewest black nodes for which the coequalizer $e$ is a monomorphism.
For instance, if, instead of $f$, we had taken the morphism
\[ g : \text{seg}_{18} \to (\circ)(\bullet)(\circ\circ)(\bullet)(\circ\circ\circ\circ\circ\circ\circ) \]
then the pairs $(c, g)$ and $(p_5, g)$ would have had the same image via $\sigma''(\text{seg}_{18}') : \text{Lan}_T(\text{seg}_{18}') \to 2E_1(\text{seg}_{18}')$, but would have been associated with different phenotypes. This would have forced the identity $\text{dis} = \text{hea}$ in the codomain of the coequalizer $e : F\Delta S \Rightarrow Q$ at the segment $\text{seg}_{18}''$. In other words, the ic-monoid $Q(\text{seg}_{18}'')$ would have been isomorphic to the terminal ic-monoid and $e$ would not have been a monomorphism at $\text{seg}_{18}''$.

Finally, note that while the segment $\text{seg}_{18}'$ seems to be optimally minimal, its topology does not precisely tell us where the variations responsible for the phenotype $\text{dis}$ are. For instance, we could try to learn more about the localization of these variations by using the two Cartesian projections $\kappa_1 : 2E_1 \Rightarrow E_1^2$ and $\kappa_2 : 2E_1 \Rightarrow E_1^2$. In this case, we would need to repeat the previous reasoning by using the following span in $[\text{Seg}(\Omega), \text{Icm}]$ for every $i \in \{1, 2\}$:

\[
\begin{array}{ccc}
F\text{Lan}_T & \xrightarrow{F\sigma''} & F2E_1 \\
\mu_{F\sigma''} & & \mu_{F\sigma''} \\
\downarrow & & \downarrow \\
F\Delta S & & F\Delta S
\end{array}
\]

We would eventually find out that the phenotype $\text{dis}$ is caused by mutations occurring on the two alleles of the individuals. Indeed, taking the first projection $\kappa_1$ would lead to forcing an identity $\text{hea} = \text{dis}$ in the codomain of the coequalizer $e : F\Delta S \Rightarrow Q$ at the segment $\text{seg}_{18}$ as the images of the pairs $(c, f)$ and $(p_{12}, f)$ through the function
\[ (\kappa_1 \circ F\sigma''_{\text{seg}_{18}}) : \text{Lan}_T(\text{seg}_{18}) \to E_1^2(\text{seg}_{18}') \]
are equal, but the phenotypes of $(c, f)$ and $(p_{12}, f)$ are different. We would reach a similar conclusion by using the second projection $\kappa_2$ and the pairs $(c, f)$ and $(p_4, f)$. This tells us that one allele is not enough to cause the disease that Charles undergoes and variations on the two alleles are probably necessary to cause the disease in general.

Note that we have been able to draw the previous conclusions because we had enough data, but the reader should understand that it is only the absence of monomorphism that informs us about the characteristics of the disease. Monomorphisms only indicate that one is on the right path to localizing the cause of the phenotype under study, but do not give much more.

In the sequel, we shall use monomorphisms to detect or force other types of mechanisms. Section 4.5 recalls some important properties about this type of morphism.

4.5. Reminder on monomorphisms and epimorphisms. In this section, we recall a few facts on how to detect epimorphisms and monomorphisms. These properties will be particularly useful to prove one of our main results (see Theorem 4.54). First, recall that a monomorphism in a category $\mathcal{C}$ is an arrow $m : A \to B$ such that for every pair of parallel arrows $f, g : X \rightrightarrows A$ for which the equation $m \circ f = m \circ g$ holds, the two arrows $f$ and $g$ must be equal.

**Proposition 4.20.** If $\mathcal{C}$ has pullbacks, then an arrow $m : A \to B$ is a monomorphism in $\mathcal{C}$ if the pullback $p_1, p_2 : P \rightrightarrows A$ of two copies of $m$ is such that $p_1$ equals $p_2$.

**Proof.** For every pair of parallel arrows $f, g : X \rightrightarrows A$ for which the equation $m \circ f = m \circ g$ holds, the universality of the pullback $P$ gives an arrow $h : X \to P$ for which the identities $f = p_1 \circ h$ and $g = p_2 \circ h$ hold. Because $p_1 = p_2$, we have $f = g$ and the statement follows. \[\square\]

**Definition 4.21** (Restricted monomorphisms). Let $I$ be an object in a category $\mathcal{C}$. A morphism $m : X \to Y$ in $\mathcal{C}$ will be said to be an $I$-monomorphism if for every pair of arrows $f, g : I \rightrightarrows X$ in $\mathcal{C}$ for which the equation $m \circ f = m \circ g$ holds, the two arrows $f$ and $g$ are equal in $\mathcal{C}$. 
Proposition 4.22. In the category $\text{Icm}$, an arrow is a monomorphism if and only if it is a $B_2$-monomorphism (see Example 4.5).

Proof. By definition, monomorphisms in $\text{Icm}$ must be $B_2$-monomorphisms. Conversely, Example 4.8 implies that $B_2$-monomorphisms $f : (M, +_M, 0_M) \to (N, +_N, 0_N)$ are given by injective functions $f : M \to N$. Because injections are monomorphisms in $\text{Set}$, we can directly check that injective morphisms in $\text{Icm}$ are monomorphisms in $\text{Icm}$ (see section 4.2). □

Now, recall that an epimorphism in a category $C$ is an arrow $e : A \to B$ such that for every pair of parallel arrows $f, g : B \Rightarrow X$ for which the equation $f \circ e = g \circ e$ holds, the two arrows $f$ and $g$ must be equal.

Definition 4.23 (Orthogonality). A morphism $f : X \to Y$ in a category $C$ will be said to be orthogonal to an object $I$ in $C$ if for every arrow $i : I \to Y$ in $C$, there exists a dashed arrow (called the lift) making the diagram given below commute in $C$.

\[
\begin{array}{c}
X \\
\downarrow^e \\
Y \\
\end{array}
\begin{array}{c}
I \\
\downarrow^i \\
Y \\
\end{array}
\]

Proposition 4.24. Every morphism in $\text{Icm}$ that is orthogonal with respect to the Boolean ic-monoid $B_2$ (Example 4.5) is an epimorphism.

Proof. We can use Example 4.8 to see that if an arrow $e : X \to Y$ is orthogonal with respect to the Boolean ic-monoid $(B_2, +, 0)$, then it is surjective: for every $y \in Y$, there exists $x \in X$ for which the identity $e(x) = y$ holds. Because surjections are epimorphisms in $\text{Set}$, we can directly check that surjective morphisms in $\text{Icm}$ are epimorphisms in $\text{Icm}$ (see section 4.2). □

4.6. Coequalizers of ic-monoids. Non-expert readers may want to look at the classical literature, say [17, def. 7.2.1.4], to review the notion of coequalizer in $\text{Set}$. The main idea behind forming coequalizers in $\text{Icm}$ is to add equations to the monoids.

Definition 4.25 (Coequalizers). Let $f, g : X \Rightarrow Y$ be a pair of morphisms in some category $C$. A coequalizer for the pair $(f, g)$ is an arrow $e : Y \to Q$ in $C$ such that

- the identity $e \circ f = e \circ g$ holds;
- for any other morphism $h : X \to Q'$ for which the identity holds $h \circ f = h \circ g$, there exists a unique arrow $h' : Q \to Q'$ making the following diagram commute.

\[
\begin{array}{c}
Y \\
\downarrow^e \\
Q \\
\end{array}
\begin{array}{c}
Q' \\
\downarrow^{h'} \\
Q' \\
\end{array}
\]

Convention 4.26. From now on, we shall follow the conventions of the literature and say that the following diagram commutes whenever the identity $e \circ f = e \circ g$ holds.

\[
\begin{array}{c}
X \\
\downarrow^f \\
Y \\
\end{array}
\begin{array}{c}
Y \\
\downarrow^g \\
Q \\
\end{array}
\]

It is well-known that the category $\text{Icm}$ is isomorphic to the category of semimodules over the Boolean semiring $[4, 16]$. While there does not seem to be any specific references describing the coequalizers of idempotent commutative monoids, the previous references give an explicit description of the coequalizers of Boolean semimodules. In the remainder of this section, we give an explicit description of the coequalizers of $\text{Icm}$ by following the constructions given thereof.
Definition 4.27 (Quotient). For every pair of morphisms \( f, g : (X, +_X, 0_X) \Rightarrow (Y, +_Y, 0_Y) \) in \( \text{Icm} \), define the binary relation \( R(f, g) \) on \( Y \) containing the pair of elements \((m, m')\) in \( Y \times Y \) such that for every ic-monoid \((Z, +_Z, 0_Z)\) and morphism \( h : (Y, +_Y, 0_Y) \rightarrow (Z, +_Z, 0_Z) \) in \( \text{Icm} \) for which the equation \( h \circ f = h \circ g \) holds, the relation \( h(m) = h(m') \) holds too.

Remark 4.28 (Equivalence relation). For every pair of arrows \( f, g : (X, +_X, 0_X) \Rightarrow (Y, +_Y, 0_Y) \) in \( \text{Icm} \), the binary relation \( R(f, g) \) on \( Y \) is obviously an equivalence relation. Below, we use the notation \([m]_{f,g}\) to denote the equivalence class of an element \( m \) in \( Y \) for this relation.

Proposition 4.29. For the same notations as those used in Definition 4.27, the quotient set \( Y/R(f, g) \) defines an ic-monoid for the addition \([m]_{f,g} + [m']_{f,g} := [m +_Y m']_{f,g}\) and the obvious zero element \([0_Y]_{f,g}\). The quotient map \( e : Y \rightarrow Y/R(f, g) \) then defines a morphism of monoids.

Proof. To show that the quotient \( Y/R(f, g) \) defines an ic-monoids, we only need to show that the addition \([m]_{f,g} + [m']_{f,g} := [m +_Y m']_{f,g}\) is well-defined – all the other axioms then follow from those of \((Y, +_Y, 0_Y)\) easily. To do so, let \((m_1, m'_1)\) and \((m_2, m'_2)\) be two pairs in \( R(f, g) \). Then, for every morphism \( h : (Y, +_Y, 0_Y) \rightarrow (Z, +_Z, 0_Z) \) in \( \text{Icm} \) for which the equation \( h \circ f = h \circ g \) as well as the relations \( h(m_1) = h(m'_1) \) and \( h(m_2) = h(m'_2) \) hold, we also have the following equations.

\[
h(m_1 +_Y m_2) = h(m_1) +_Z h(m_2) = h(m'_1) +_Z h(m'_2) = h(m'_1 +_Y m'_2)
\]

This shows that \((m_1 +_Y m_2, m'_1 +_Y m'_2)\) is also in \( R(f, g) \) and that \((Y/R(f, g), +, [0_Y]_{f,g})\) is well-defined as an ic-monoid. The quotient map \( e : Y \rightarrow Y/R(f, g) \) defines a morphism of monoids by definition of the ic-monoid structure given to \( Y/R(f, g) \).

Proposition 4.30. Let \( f, g : X \Rightarrow Y \) be a pair of morphisms in \( \text{Icm} \). The morphism \( e : Y \rightarrow Y/R(f, g) \) defines the coequalizer of \((f, g)\) in \( \text{Icm} \).

Proof. The existence property of the universal property directly follows from the way the relation \( R(f, g) \) is defined (see Definition 4.27) while its uniqueness property follows from the surjectiveness of the function \( e : Y \rightarrow Y/R(f, g) \) as a quotient map of sets (Proposition 4.29).

Remark 4.31 (Orthogonality). Let \( f, g : X \Rightarrow Y \) be a pair of morphisms in \( \text{Icm} \). Since the coequalizer \( e : Y \rightarrow Y/R(f, g) \) of \((f, g)\) is surjective, by definition of a quotient map of sets (see Proposition 4.29), it follows from Example 4.8 that \( e : Y \rightarrow Y/R(f, g) \) is orthogonal to the ic-monoid \((B_2, +, 0)\).

4.7. Predicting phenotypes with haplotypes. In section 4.4, we saw how the concept of sequence alignment could be used to link genotypes to phenotypes via a span structure in the category \( \text{Icm} \) (see Remark 4.18). In Example 4.19, we saw how this span structure could be used with coequalizers and the concept of monomorphism to localize the variations responsible for a phenotype. Our goal is now to show how one can use the span structure of Remark 4.18 to predict the phenotype of a genotype that is not part of our dataset.

The idea is that a given individual is likely to have a certain type of phenotype if its relatives possess it too. Therefore, a way to predict the phenotype of a given genotype would be to look at the phenotypes of a set of genotypes that could give rise to the given genotype up to recombination over several generations. More specifically, we want to look at genotypes from the point of view of their haplotypes.

```
[ a genotype ] is part of [ a haplogroup ] which has a [ a haplotype ]
```

Recall that, in genetics, a haplotype is a given set of genes or DNA strands, say ACCTA and TAG, for particular loci on a chromosome while a haplogroup for this haplotype can be viewed as a group of DNA segments sharing these strands at the specified locations whereas the other locations
may contain SNPs (see also section 2.1). The following diagram give an example of a set of three haplogroups for three different haplotypes. Two of the haplogroups are sub-haplogroups of the third one.

\[
\begin{array}{c}
\text{haplotype} \\
ACGA : TAG
\end{array} \quad \begin{array}{c}
\text{haplogroup} X \\
\ldots \text{ACGA}(A \text{ or } C)\text{TAG}(T \text{ or } C) \ldots
\end{array} \quad \begin{array}{c}
\text{haplotype} \\
ACGAATAG
\end{array} \quad \begin{array}{c}
\text{haplogroup} XA \\
\ldots \text{ACGAATAG}(T \text{ or } C) \ldots
\end{array} \quad \begin{array}{c}
\text{haplotype} \\
ACGAATAG
\end{array} \quad \begin{array}{c}
\text{haplogroup} XC \\
\ldots \text{ACGAATAG}(T \text{ or } C) \ldots
\end{array} \quad \begin{array}{c}
\text{haplotype} \\
ACGACTAG
\end{array}
\]

In this paper, we formalize the concept of haplotype, haplogroup and genotype as follows.

**Definition 4.32** (Genotypes, haplotypes and haplogroups). Let \((\Omega, \preceq)\) be a pre-ordered set and \(X : \text{Seg}(\Omega) \to \text{Set}\) be a functor. For every cone \(\rho : \Delta_A(\tau) \Rightarrow \theta\) (section 2.8) in \(\text{Seg}(\Omega)\), a limit adjoint of the image of \(\rho\) via the functor \(FX : \text{Seg}(\Omega) \to \text{Icm}\) is a canonical arrow of the following form in \(\text{Icm}\) (for a choice of limit).

\[
FX(\tau) \to \lim_A FX \circ \theta
\]

In the sequel, we shall call
1) a \(\rho\)-**genotype** an element in the set \(X(\tau)\);
2) a \(\rho\)-**haplotype** an element in the ic-monoid \(\lim_A FX \circ \theta\);
3) a \(\rho\)-**haplogroup** for a certain \(\rho\)-haplotype \(x\) an element in the ic-monoid \(FX(\tau)\) whose image via (4.6) is \(x\).

**Example 4.33** (Genotypes, haplotypes and haplogroups). Let \((\Omega, \preceq)\) be the Boolean pre-ordered set \(\{0 \leq 1\}\) and let \((E, \varepsilon)\) be our usual pointed set \(\{A, C, G, T, \varepsilon\}\). Take \(\rho : \Delta_A(\tau) \Rightarrow \theta\) to be the following cone in \(\text{Seg}(\Omega)\).

\[
\begin{array}{ccc}
(\ldots\ldots\ldots\ldots\ldots)(o)(\ldots\ldots\ldots) \\
\uparrow
\end{array} \quad \begin{array}{ccc}
(\ldots\ldots\ldots\ldots\ldots)(\bullet)(\ldots\ldots\ldots) \\
\downarrow
\end{array}
\begin{array}{c}
(\ldots\ldots\ldots\ldots\ldots)(\bullet)(\ldots\ldots\ldots) \\
(\ldots\ldots\ldots\ldots\ldots)(o)(\ldots\ldots\ldots)
\end{array}
\]

The elements of \(F^2 E^2_{\tau}(\tau)\) given in the left column of the following table (parentheses were added for clarity) are all \(\rho\)-genotypes. Their images through the canonical arrow \(F^2 E^2_{\tau}(\tau) \to \prod_{i \in [k]} F^2 E^2_{\tau}(\theta(i))\) are given in the right column – they correspond to their haplotypes.

| in \(F^2 E^2_{\tau}(\tau)\) | in \(\prod_{i \in [k]} F^2 E^2_{\tau}(\theta(i))\) |
|--------------------------|---------------------------------|
| a = (ACCATTAG)(C)(TAC)(CTATAC) (ACCACTAG)(C)(TAC)(ATATGC) | (ACCATTAG) (C) (TAC) (ACCACTAG) (C) (TAC) |
| b = (AGCATTAG)(G)(TTC)(GTATGC) (ACCACTAG)(C)(TAC)(CTATTC) | (AGCATTAG) (G) (TTC) (ACCACTAG) (C) (TAC) |
| \(P_{10}\) = (ACCATTAG)(G)(TAC)(ATATGC) (ACCACTAG)(C)(TAC)(CTATTC) | (ACCATTAG) (G) (TAC) (ACCACTAG) (C) (TAC) |
| \(P_2\) = (AGCATTAG)(C)(TTC)(GTATGC) (ACCACTAG)(C)(TAC)(ATATGC) | (AGCATTAG) (C) (TTC) (ACCACTAG) (C) (TAC) |

Since the canonical arrow \(F^2 E^2_{\tau}(\tau) \to \prod_{i \in [k]} F^2 E^2_{\tau}(\theta(i))\) is a morphism of ic-monoids (see Remark 4.10 for the monoid structure of products), we deduce from the previous table that the element
$a + p_{10}$ is a $\rho$-haplogroup of the following $\rho$-haplotype.

\[
\begin{pmatrix}
\text{ACCATTAG} & (C) \\
\text{ACCATTAG}' & (C) \end{pmatrix} + 
\begin{pmatrix}
\text{G} & \text{TAC} \\
\text{G} & \text{TAC}'
\end{pmatrix}
\]

Similarly, the sum $b + p_2$ is a $\rho$-haplogroup for the following $\rho$-haplotype.

\[
\begin{pmatrix}
\text{AGCATTAG} & (C) \\
\text{AGCATTAG}' & (C) \end{pmatrix} + 
\begin{pmatrix}
\text{C} & \text{TAC} \\
\text{C} & \text{TAC}'
\end{pmatrix}
\]

Finally, the element $a + p_{10} + b + p_2$ is a $\rho$-haplogroup for the following $\rho$-haplotype, which is a sup-haplotype of the previous two.

\[
\begin{pmatrix}
\text{AGCATTAG} & (C) \\
\text{AGCATTAG}' & (C) \end{pmatrix} + 
\begin{pmatrix}
\text{AGCATTAG} & (C) \\
\text{AGCATTAG}' & (C) \end{pmatrix} + 
\begin{pmatrix}
\text{G} & \text{TAC} \\
\text{G} & \text{TAC}'
\end{pmatrix} + 
\begin{pmatrix}
\text{C} & \text{TAC} \\
\text{C} & \text{TAC}'
\end{pmatrix}
\]

One thing that Example 4.33 do not quite capture is the law of segregation, which may make the inheritance of a certain haplotype more complex than a mere transmission of the two alleles from parents to children, mostly over several generations.

Indeed, recall that the recombination of the chromosomes of two individuals goes as follows. First, each chromosome of the pair of chromosomes possessed by the two individuals are separated from each other – this is the first law of Mendelian inheritance: the law of segregation.

\[
\begin{pmatrix}
\text{ACCATTAGCTACCTATAC} \\
\text{ACCACCTAGCTACATATGC}
\end{pmatrix} \Rightarrow 
\begin{pmatrix}
\text{ACCATTAGCTACCTATAC} \\
\text{ACCACCTAGCTACATATGC}
\end{pmatrix}
\]

Then, the separated chromosomes are cut in various locations and shuffled between each other so that the positions of each part of the chromosomes are essentially preserved.

It is only then that the chromosomes of the two different individuals meet during reproduction. Over several generations, this shuffling usually lead to a set of chromosomes much more diversified than the set of chromosomes that would be obtained by shuffling the two chromatides of the chromosome together. The following definition aims to model the law of segregation as a natural transformation.

**Definition 4.34** (Law of segregation). Let $b$ be an element in $\Omega$. We will denote by $\text{sgg}$ the natural transformation $2E_b \Rightarrow UFE_b$ in $[\text{Seg}(\Omega), \text{Icm}]$ that is obtained, for every segment $\tau$ in $\text{Seg}(\Omega)$, from the composition of the sequence of arrows displayed in (4.7), where

- the leftmost arrow is the product of two copies of the unit of adjunction (4.1);
- the middle arrow is the isomorphism making the right adjoint $U$ commute with products;
- the rightmost arrow is the image of the natural transformation of Remark 4.11 via $U$;

\[
(4.7) \quad E_b^\tau(\tau) \times E_b^\tau(\tau) \xrightarrow{\eta_b \times \eta_b} UFE_b(\tau) \times UFE_b(\tau) \xrightarrow{= U(FE_b(\tau) \times FE_b(\tau))} U(FE_b(\tau) \times FE_b(\tau)) \xrightarrow{U\text{sum}} UFE_b(\tau)
\]

Note that the naturality of this arrow in $\tau$ is straightforward from the structures used.
Remark 4.35 (First Mendelian law). For every element $b$ in $\Omega$, we can use the universal property of adjunction (4.1) to show that the morphism $sgg : 2E^\varepsilon_b \Rightarrow UFE^\varepsilon_b$ extends to a morphism $fnl : F2E^\varepsilon_b \Rightarrow FE^\varepsilon_b$ (whose name stands for first Mendelian law) in $[\text{Seg}(\Omega), \text{Icm}]$.

\[
\begin{array}{c}
2E^\varepsilon_b \xrightarrow{sgg} UFE^\varepsilon_b \\
\eta 2E^\varepsilon_b \Downarrow \varepsilon \Rightarrow U(fnl)
\end{array}
\]

Then, we can use $fnl : F2E^\varepsilon_b \Rightarrow FE^\varepsilon_b$ to extend the rightmost span of (4.4) as follows.

\[
\begin{array}{c}
F\text{Lan}_T \xrightarrow{\mu F\sigma^*} F2E^\varepsilon_b \xrightarrow{fml} FE^\varepsilon_b \\
\mu F\varphi \Downarrow F\Delta S
\end{array}
\]

Later, we shall use this span to predict the phenotype of a given genotype up to homologous recombination. Before doing so, we will need to coequalize the object $FE^\varepsilon_b$ with respect to certain congruences, which are defined in section 4.8.

Let us now address the title of the present section, namely the prediction of phenotypes. Ideally, we would like to formalize the prediction process in terms of an epimorphism

\[
f : \text{Phenotypes} \to \text{Haplotypes}
\]

that would lift every haplotype to, at least, one phenotype so that every individual $p$ of a certain haplotype $x$ can be associated with a fiber of possible phenotypes $f^{-1}(x)$.

Unfortunately, in the present context, our knowledge is limited to the observations made for our sample of individuals. This limitation makes epimorphism (4.8) difficult to construct in its full form. In fact, the best we can hope to achieve is to construct an epimorphism

\[
f' : \text{Observation} \to \text{Haplotypes}^*
\]

going from the set of observed phenotypes to the set of predictable haplotypes, which consists of all those haplotypes that can be generated from the genetic data of our sample.

To make sure that epimorphism (4.9) really captures what epimorphism (4.8) is supposed to model, we will need to show that what we understand as “predictable haplotypes” can be embedded into a world of actual haplotypes – this is where the concept of pedigrad is needed (to be continued in Remark 4.44).

4.8. Recombination chromologies. We shall speak of a recombination chromology to refer to a chromology $(\Omega, D)$ such that, for every non-negative integer $n$, the set $D[n]$ is finite and only contains wide spans (see Definition 2.16).

Example 4.36 (Examples and non-example). Let $\Omega$ denote the pre-ordered set $\{0 \leq 1\}$. The following diagram, in one of the pre-order categories $\text{Seg}(\Omega : t)$ for the obvious topology $t$ of domain [12], is an example of a cone suitable for a recombination chromology.

\[
\begin{array}{c}
(o)(o)(o)(o) \\
(o)(o)(o)(o) \\
(o)(o)(o)(o)
\end{array}
\]
From a biological point of view, this type of cone could be used to specify how homologous recombination operates on the patches of a given segment.

The following diagram in the category of quasi-homologous segments $\text{Seg}(\Omega | 12)$ is another example.

The difference between the very first cone and the one given above is that the latter specifies an operation whose action extends to a more refined topology. For instance, even though homologous recombination acts on genes, it also acts on codons because genes can be described as sequences of codons.

An example of a cone that is not suitable for a recombination chromology is given below, where the small category on which the cone is defined is a cospan $A = \{ \cdot \to \cdot \leftarrow \cdot \}$.

$\text{Convention 4.37 (Notation).}$ Let $(\Omega, D)$ be a recombination chromology and $X$ be a functor $\text{Seg}(\Omega) \to \text{Icm}$. For every wide span $\rho : \Delta_{[k]}(\tau) \Rightarrow \theta$ in $(\Omega, D)$, the limit adjoint of the wide span $X(\rho) : X\Delta_{[k]}(\tau) \Rightarrow X\theta$ in $\text{Icm}$, for the product structure defined in Remark 4.10, will be denoted as follows.

$X[\rho] : X(\tau) \to \prod_{i \in [k]} X\theta(i)$

$\text{Definition 4.38 (Recombination congruences).}$ Let $(\Omega, D)$ be a recombination chromology and $X$ be a functor $\text{Seg}(\Omega) \to \text{Icm}$. For every wide span $\rho : \Delta_{[k]}(\tau) \Rightarrow \theta$ in $(\Omega, D)$, we will denote by $G(X, \rho)$ the pullback of the arrow $X[\rho]$ along itself (see below) and call the resulting pair arrows $G(X, \rho) \Rightarrow X(\tau)$ the recombination congruence of $X$ on $\rho$.

$\text{Example 4.39 (Recombination congruences).}$ Let $(\Omega, \preceq)$ be the Boolean pre-ordered set $\{0 \leq 1\}$ and let $(E, \varepsilon)$ be our usual pointed set $\{ A, C, G, T, \varepsilon \}$. Take $\rho$ to be the wide span of homologous segments given below; the small discrete category $A$ on which $\rho$ is defined will be taken to be
equal to the finite set \{a_1, a_2, a_3\}.

\[
\begin{array}{c}
(\bullet\bullet\bullet\bullet\bullet)(\circ\circ\circ\circ\circ)(\circ\circ\circ\circ\circ) \quad \theta(a_1) \\
(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet) \quad \theta(a_2) \\
(\circ\circ\circ\circ\circ)(\circ\circ\circ\circ\circ)(\bullet\bullet\bullet\bullet\bullet) \quad \theta(a_3)
\end{array}
\]

The idea behind the notion of recombination congruence is that the ic-monoid \(G(FE_1^\varepsilon, \rho)\) contains the pairs of elements of \(FE_1^\varepsilon(\rho)\) that are the same up to homologous recombination, over an indefinite number of generations, with respect to the topology specified by the cone \(\rho\).

For instance, consider the elements of \(FE_1^\varepsilon(\tau)\) given in the following table, which are the images of the elements \(a, b, c, p_4, p_5\) and \(p_6\) of Example 3.10 through the first law of Mendelian inheritance \(fml : F2E_b^\varepsilon \Rightarrow FE_b^\varepsilon\) defined in Remark 4.35.

| \(a\) | \(b\) | \(c\) | \(p_4\) | \(p_5\) | \(p_6\) |
| --- | --- | --- | --- | --- | --- |
| \((\text{ACCATT})(\text{AGCTAC})(\text{CTATAC}) + (\text{ACCACT})(\text{AGCTAC})(\text{ATATGC})\) | \((\text{AGCATT})(\text{AGGTTC})(\text{GTATGC}) + (\text{ACCACT})(\text{AGGTTC})(\text{CTATAC})\) | \((\text{AACATT})(\text{AGGTTC})(\text{TTATAC}) + (\text{ACCACT})(\text{AGGTTC})(\text{ATATGC})\) | \((\text{AACATT})(\text{AGGTTC})(\text{GTATGC}) + (\text{ACCACT})(\text{AGGTTC})(\text{ATATTC})\) | \((\text{AACATT})(\text{AGGTTC})(\text{GTATGC})\) |

We can check that the \(\rho\)-haplotypes of the previous elements are equal to the following tuples.

| \(a\) | \(b\) | \(c\) | \(p_4\) | \(p_5\) | \(p_6\) |
| --- | --- | --- | --- | --- | --- |
| \((\text{ACCATT} + \text{ACCACT} + \text{AGCTAC} + \text{CTATAC} + \text{ATATGC})\) | \((\text{AGCATT} + \text{ACCACT} + \text{AGGTTC} + \text{AGCTAC} + \text{GTATGC} + \text{CTATAC})\) | \((\text{AACATT} + \text{ACCACT} + \text{AGGTTC} + \text{CTATAC} + \text{ATATGC} + \text{ATATTC})\) | \((\text{AACATT} + \text{ACCACT} + \text{AGGTTC} + \text{AGCTAC} + \text{GTATGC} + \text{ATATTC})\) | \((\text{AACATT} + \text{ACCACT} + \text{AGGTTC} + \text{GTATGC} + \text{ATATTC})\) |

We can use the previous table to deduce that the \(\rho\)-haplotype of the sum \(b + c\) is equal to the \(\rho\)-haplotype of the sum \(p_4 + p_6\). In other words, the pair \((b + c, p_4 + p_6)\) is an element of the ic-monoid \(G(FE_1^\varepsilon, \rho)\).

On the other hand, the \(\rho\)-haplotype of the element \(p_4 + p_5 + p_6\) is not equal to the \(\rho\)-haplotype of the sum \(b + c\) (see the sequence \(\text{AGGTTC}\) that only appears for \(p_5\)). In fact, it is not even equal to the \(\rho\)-haplotype of the sum \(a + b + c\) via \(FE_1^\varepsilon(\rho)\), which contradicts the fact that \(p_5\) describes the genetic data of an individual in the progeny of \text{Alice}, \text{Brian} and \text{Charles}. This tells us that the previously considered cone may give the wrong topology for the recombination operation that lead to \(p_5\). In other words, the arrow of Convention 4.37 makes it possible to identify the regions at which crossovers cannot have occurred by looking at the cones for which equations of the form \(a + b + c + p = p\) fail to hold (as is the case for \(p = p_3\)).

In general, the hot spots at which crossovers occur in the human genome do not change much and only their occurrence frequency does [7]. For instance, there may be a noticeable difference in male and female regarding the frequency at which certain hot spots are used, but the hot spots will essentially be the same for both genders. However, topologies may change between different species (see [7]).

In the case of our example, we will suppose that the progeny of \text{Alice}, \text{Brian} and \text{Charles} was produced for the same topology. The reader may verify that the following new cone \(\rho' :
\[ \Delta_A(\tau) \Rightarrow \theta' \] does not lead to any such failure for the previous elements.

Indeed, the \( \rho' \)-haplotypes of the elements \( a, b, c, p_4, p_5, \) and \( p_6 \) are equal to the following tuples:

\[
\begin{array}{c|c}
\hline
 & \text{in } \prod_{i \in [k]} \mathcal{E}_i' \theta'(i) \\
 a & (\text{ACCATT} + \text{ACCACT}, \text{AGC}, \text{TACCTATAC} + \text{TACATATGC}) \\
b & (\text{AGCATT} + \text{ACCACT}, \text{AGG + AGC}, \text{TTCGTATGC + TACCTATTC}) \\
c & (\text{AACATT} + \text{ACCACT}, \text{AGG}, \text{TTCCTTATAC} + \text{TTCATATTC}) \\
p_4 & (\text{AGCATT} + \text{ACCACT}, \text{AGG + AGC}, \text{TTCGTATGC + TACCTATTC}) \\
p_5 & (\text{AACATT} + \text{ACCACT}, \text{AGG}, \text{TTCCTTATAC + TTCGTATGC}) \\
p_6 & (\text{AACATT} + \text{ACCACT}, \text{AGG}, \text{TTCCTTATAC + TTCGTATGC}) \\
\hline
\end{array}
\]

Here, we can see that the \( \rho' \)-haplotype of the sum \( b + c \) is equal to the \( \rho' \)-haplotype of the sum \( p_4 + p_5 + p_6 \), which means that the pair \( (b + c, p_4 + p_5 + p_6) \) belongs to the ic-monoid \( G(\mathcal{E}_i', \rho') \).

Example 4.39 has showed that it is possible to detect ‘good’ cones for a given data set by looking at the haplotypes generated by these cones. These cones should ideally be gathered within a recombination chromology. In section 4.9, we see how one can use such a chromology to give a meaning to the sentence “up to recombination”.

### 4.9. Recombination monoids

The goal of the present section is to define the quotient of a functor \( \text{Seg}(\Omega) \rightarrow \text{Icm} \) with respect to a set of recombination congruences (Definition 4.38). We start the section with a discussion on how to form functorial quotients.

**Remark 4.40 (Functorial quotients).** Let \( (\Omega, \preceq) \) be a pre-ordered set, \( (\Omega, D) \) be a recombination chromology and \( X \) be a functor \( \text{Seg}(\Omega) \rightarrow \text{Icm} \). To quotient the functor \( X \) with respect to its recombination congruences \( G(X, \rho) \Rightarrow X(\tau) \) over its cones \( \rho : \Delta_A(\tau) \Rightarrow \theta \) in \( D \), we could consider the coequalizer, call it \( Q(\tau) \), of the coproduct adjoint of the collection of all its recombination congruences, as shown below.

\[
\prod_{\rho \in D} G(X, \rho) \xrightarrow{\oplus_{\rho \preceq 1}} X(\tau)
\]

Because the resulting mapping \( \tau \mapsto Q(\tau) \) is unlikely to be functorial, the idea is to force the functoriality by adding more pairs to the previous coproduct. Specifically, we need to consider the pair of arrows resulting from the composition of the rightmost arrow of (4.10) with the pair of arrows shown on its left: the coproduct is this time taken over the finite set of pairs \( (\rho, f) \) where \( \rho \) is a cone of the form \( \Delta_A(\upsilon) \Rightarrow \theta \) in \( D \) and \( f \) is an arrow \( \upsilon \rightarrow \tau \) in \( \text{Seg}(\Omega) \).

\[
\prod_{\rho, f : \upsilon \rightarrow \tau} G(X, \rho) \xrightarrow{\oplus_{\rho \preceq 1}} \prod_{\rho, f : \upsilon \rightarrow \tau} X(\upsilon) \xrightarrow{\oplus_{\rho \preceq 2}} X(\tau)
\]
Then, for every morphism \( g : \tau \to \tau' \), we can define the following diagram, which makes the coequalizer of (4.10) an obvious functor on \( \text{Seg}(\Omega) \).

\[
\begin{array}{c}
\coprod_{\rho,f,v \to \tau} G(X, \rho) \\
\coprod_{\rho,f,v \to \tau'} G(X, \rho)
\end{array}
\xrightarrow{\coprod_{\rho,f,v \to \tau} X(v)}
\begin{array}{c}
\coprod_{\rho,f,v \to \tau} X(v) \\
\coprod_{\rho,f,v \to \tau'} X(v)
\end{array}
\xrightarrow{\coprod_{\rho,f,v \to \tau} X(f)}
\begin{array}{c}
X(\tau) \\
X(\tau')
\end{array}
\]

**Definition 4.41** (Recombination monoids). For every recombination chromology \((\Omega, D)\) and object \(\tau\) in \( \text{Seg}(\Omega) \), we will denote by \( DX(\tau) \) the coequalizer of (4.10). The associated functor \( DX : \text{Seg}(\Omega) \to B_2\text{-Mod} \) will be called the recombination monoid of \((\Omega, D)\) over \(X\).

**Convention 4.42** (Coequalizer map). For every functor \( X : \text{Seg}(\Omega) \to \text{Set} \), the coequalizer map \( X \to DX \) associated with the coequalizer of diagram (4.10) will be denoted as \( q_X \).

**Example 4.43** (Recombination monoids). Let \((E, \varepsilon)\) be our usual pointed set \(\{A, C, G, T, \varepsilon\}\) and take \((\Omega, \preceq)\) to be the Boolean pre-ordered set \(\{0 \leq 1\}\). In Example 4.39, we showed how the choice of certain cones \(\rho : \Delta_A(\tau) \Rightarrow \theta\) could change the way the elements of \(F E_1^\tau(\tau)\) are identified through the canonical arrow \(FE_1^\tau[\rho] : FE_1^\tau(\tau) \to \bigoplus_{i \in [k]} FE_1^\tau(\theta(i))\). In the case of the recombination monoids, these identification are realized as equations.

Suppose that the cone \(\rho : \Delta_A(\tau) \Rightarrow \theta\) given in Example 4.39 is one of the cones contained in \(D\), then the coequalizer map \( q_{FE_1^\tau} : FE_1^\tau(\tau) \to DFE_1^\tau(\tau) \) will identify the two elements \(b + c\) and \(p_4 + p_6\), which are distinct elements of \(FE_1^\tau(\tau)\), as a single element in \(DFE_1^\tau(\tau)\). In other words, the following identity will hold in \(DFE_1^\tau(\tau)\).

\[
b + c = p_4 + p_6
\]

Similarly, if we suppose that the cone \(\rho' : \Delta_A(\tau') \Rightarrow \theta'\) given in Example 4.39 is another cone of \(D\), then the coequalizer map \( q_{FE_1^\tau} : FE_1^\tau(\tau') \to DFE_1^\tau(\tau') \) will identify the two elements \(a + b + c\) and \(p_4 + p_5 + p_6\), which are also distinct in \(FE_1^\tau(\tau')\), as a single element in \(DFE_1^\tau(\tau')\), thus giving the following identity.

\[
a + b + c = p_4 + p_5 + p_6
\]

More generally, for any cone \(\rho\) in \(D\), the coequalizer of diagram (4.10) will force the two components of a pair contained in \(G(\tau)\) to be identified in the recombination monoid \(DFE_1^\tau(\tau)\).

**Remark 4.44** (From genotype to phenotype). Let \((\Omega, \preceq)\) be a pre-ordered set, \((\Omega, D)\) be a recombination chromology, \(b\) be an element of \(\Omega\), \((E, \varepsilon)\) be a pointed set and \((\iota, T, \sigma)\) be a sequence alignment over \(2E_0^\varepsilon\). Consider a phenotypic expression for \((\iota, T, \sigma)\) given by a morphism \(\varphi : T \Rightarrow UF\Delta S \circ \iota\) as well as the associated span constructed at the end of Remark 4.35 for this phenotypic expression, namely the lefmost span of (4.4) with which the first mendelian law morphism \(\text{fnl} : F^2E_0^\varepsilon \Rightarrow FE_1^\varepsilon\) is composed (see below, on the left).

\[
\begin{array}{c}
F \Lambda \iota T \\
\mu F^\varphi^* \downarrow
\end{array}
\xrightarrow{\mu F^\varphi^*}
\begin{array}{c}
F F^2E_0^\varepsilon \\
\text{fnl} \downarrow
\end{array}
\xrightarrow{\text{fnl}}
\begin{array}{c}
FE_1^\varepsilon \\
\mu F \Delta S
\end{array}
\]
Composing the horizontal leg of the previous span with the coequalizer \( q_{FE_b} : FE_b \Rightarrow DFE_b \) gives the following span, whose horizontal leg is denoted as \( \text{rec} : F\text{Lan}_T \Rightarrow DFE_b \) for convenience.

\[(4.11)\]

\[
\begin{array}{cc}
\mu F \varphi^* & \mu F \varphi^* \\
\downarrow & \downarrow \\
F\text{Lan}_T & DFE_b
\end{array}
\]

Now let us denote by \( R_D^T \) the pullback of \( \text{rec} : F\text{Lan}_T \Rightarrow DFE_b \) along itself in \([\text{Seg}(\Omega), \text{Icm}]\) (see below, on the left).

\[
\begin{array}{cc}
R_D^T & y_1 \\
\downarrow y_2 & \downarrow \text{rec} \\
F\text{Lan}_T & DFE_b
\end{array}
\]

Coequalizing the resulting pullback pair then gives a coequalizer \( r : F\text{Lan}_T \Rightarrow D_E T \) (see above, on the right) whose components at given segments in \( \text{Seg}(\Omega) \) are also coequalizers in \( \text{Icm} \).

Here, we would now like to claim that this coequalizer \( r \) correspond to the epimorphism \( f' : \text{Observation} \rightarrow \text{Haplotypes}^\ast \) described at the end of section 4.7. Indeed, note that every element in the images of \( F\text{Lan}_T \) can be associated with a phenotype (i.e. an observation) via the vertical leg of span (4.11). This makes \( F\text{Lan}_T \) suitable for being seen as a space of observations. Also, note that, by Proposition 4.24 and Remark 4.31, every component of the coequalizer \( r : F\text{Lan}_T \Rightarrow D_E T \) is an epimorphism, which means that \( r \) is an epimorphism in \([\text{Seg}(\Omega), \text{Icm}]\). In the end, our claim would be proven if we could show that the object \( D_E T \) can be seen as a proper space of haplotypes – this will be the goal of section 4.10. In particular, we will show that for every cone \( \rho : \Delta_{[k]}(\tau) \Rightarrow \theta \), the arrow

\[
D_E T[\rho] : D_E T(\tau) \rightarrow \prod_{i \in [k]} D_E T\theta(i)
\]

is a monomorphism in \( \text{Icm} \). In the spirit of Definition 4.32, this would mean that the ic-monoid \( D_E T(\tau) \) can be seen as a space of \( \rho \)-haplotypes. This will be formalized by showing that \( D_E T \) is a pedigrad for a certain logical system of monomorphisms in \( \text{Icm} \) (see Corollary 4.56). Below, Example 4.45 shows what the element of \( D_E T \) look like from the point of view of our main example given in section 2.1.

**Example 4.45** (From genotype to phenotype). In this example, we show what the construction of Remark 4.44 look like in the context of Example 4.43. In this respect, we will keep the same notations and assumptions as those used thereof. We will focus on the two equations given in Example 4.43. First, the equation \( b + c = p_4 + p_6 \) of Example 4.43 is, according to the conventions of Example 4.39, equivalent to the following equations, where \( b, c, p_4 \) and \( p_6 \) are the elements of \( F\text{Lan}_T(\tau) \) given in Example 3.10.

\[
\text{rec}(b + c) = \text{rec}(b) + \text{rec}(c) = \text{rec}(p_4) + \text{rec}(p_6) = \text{rec}(p_4 + p_6)
\]
Therefore, the pair \((b + c, p_4 + p_6)\) belongs to the pullback \(R^T_{TD}(\tau)\), which obviously implies that the following equation holds in the coequalizer object \(DE\).

\[
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{TTATAC} \\
\text{ACCACT} \\
\text{AGGTTC} \\
\text{GTATGC}
\end{array}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGGTTC} \\
\text{GTATGC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGGTTC} \\
\text{AGCTAC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} = \begin{array}{c}
\text{AGCATT} \\
\text{AGCTAC} \\
\text{CTATTC} \\
\text{ACCACT} \\
\text{AGGTTC} \\
\text{GTATGC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array}.
\]

Similarly, the equation \(a + b + c = p_4 + p_5 + p_6\) leads to the following equation in \(DE\).

\[
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{TTATAC} \\
\text{ACCACT} \\
\text{AGGTTC} \\
\text{GTATGC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} = \begin{array}{c}
\text{AGCATT} \\
\text{AGCTAC} \\
\text{CTATTC} \\
\text{ACCACT} \\
\text{AGGTTC} \\
\text{GTATGC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{GTATGC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array} + \frac{1}{2}
\begin{array}{c}
\text{AGCATT} \\
\text{AGGTTC} \\
\text{ATATTC} \\
\text{ACCACT} \\
\text{AGCTAC} \\
\text{CTATTC}
\end{array}.
\]

Here, we can notice that the first Mendelian law has been able to act on the alleles of each pair of alleles, which would not have been possible if we had considered the recombination congruences of \(F_2E_9\) shown in Example 4.33.

4.10. **Recombination schemes.** The goal of this section is to show that the claim made in Remark 4.44 makes sense (see Corollary 4.56). In particular, we determine a set of conditions for which a recombination monoid, as given in Definition 4.41, is a pedigrad in a certain logical system of monomorphisms.

**Definition 4.46** (Logical system). We will denote by \(W^{\text{mon}}\) the class of wide spans \(S = \{X \to F_i\}_{i \in [k]}\) in \(Icm\) whose product adjoint arrows \(X \to \prod_{i \in [k]} F_i\) is a monomorphism in \(Icm\).

**Remark 4.47** (Homologous recombination). A \(W^{\text{mon}}\)-pedigrad is a functor in which the recombination congruences resulting from the logical system \((Icm, W^{\text{mon}})\) can be seen as identities. Another way to put it is to say that a \(W^{\text{mon}}\)-pedigrad is a functor in which homologous recombination happens (see Example 4.43).

**Definition 4.48** (Irreducibility). Let \((\Omega, D)\) be a recombination chromology and \(X\) be a functor \(\text{Seg}(\Omega) \to \text{Set}\). An object \(\tau\) in \(\text{Seg}(\Omega)\) will be said to be irreducible for the triple \((\Omega, D, X)\) if for every arrow \(f : \upsilon \to \tau\) in \(\text{Seg}(\Omega)\), the image \(X(f) : X(\upsilon) \to X(\tau)\) coequalizes the following pair of arrows for every cone \(\rho : \Delta_A(\upsilon) \Rightarrow \theta\) in \(D\).

\[
G(X, \rho) \xrightarrow{\text{pr}_j} \xrightarrow{\text{pr}_i} \]

\[
\begin{align*}
(4.12) & \\
G(X, \rho) & \xrightarrow{\text{pr}_j} \xrightarrow{\text{pr}_i} X(\upsilon)
\end{align*}
\]

**Remark 4.49** (Coequalizing arrows). By Definition 4.38, the pair of arrows given in (4.12) is coequalized by the canonical arrow \(X[\rho] : X(\upsilon) \to \prod_{i \in [k]} X \circ \theta(i)\). Since the composition of \(X[\rho]\) with the product projection

\[
\prod_{i \in [k]} X \circ \theta(i) \to X \circ \theta(j)
\]

is equal, for every \(j \in [k]\), to the morphism \(X(\rho_j) : X(\tau) \to X(\theta(j))\). This implies that, for every \(i \in [k]\), the arrow \(X(\rho_i)\) coequalizes the pair given in (4.12).
Example 4.50 (Coequalizing arrows). Let us consider the same setting as the one used in Example 4.39. We shall illustrate the concept of irreducibility by using the cone $\rho$ given thereof.

First, Remark 4.49 implies that the recombination congruence $G(FE^\epsilon_1, \rho) \Rightarrow FE^\epsilon_1(\tau)$ is co-equalized by the image of the following arrows via the functor $FE^\epsilon_1 : \text{Seg}(\Omega) \rightarrow \text{Icm}$.

\[
\begin{align*}
\rho_{a_1} & : (\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet) \rightarrow (\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet) \\
\rho_{a_2} & : (\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet) \rightarrow (\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet) \\
\rho_{a_3} & : (\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet) \rightarrow (\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet\bullet)
\end{align*}
\]

Indeed, we can check that these arrows would send the pair of equivalent elements $b + c$ and $p_4 + p_6$ that was given in Example 4.39 to the same elements, which are displayed below.

| Images of $b + c$ or $p_4 + p_6$ | $FE^\epsilon_1(\rho_{a_1})$ | $FE^\epsilon_1(\rho_{a_2})$ | $FE^\epsilon_1(\rho_{a_3})$ |
|----------------------------------|---------------------------|---------------------------|---------------------------|
|                                  | AGCATC + AGCATC + AGCATC | AGCTTC + AGCTTC + AGCTAC | GTATGC + GTATGC + TTATAC + ATATTC |

As will be shown in Proposition 4.51, this means that the codomains of the arrows $\rho_{a_1}, \rho_{a_2}$ and $\rho_{a_3}$ may be good candidates for being irreducible objects with respect to a triple of the form $\{0, 1\}, D, FE^\epsilon_1$. It is however important to understand that the domains of the arrows of a cone may not be irreducible if there is another cone in the chromology that add more pairs to the recombination congruence so that the previous property is disturbed.

Proposition 4.51. Let $(\Omega, D)$ be a recombination chromology and $X$ be a functor $\text{Seg}(\Omega) \rightarrow \text{Icm}$. Suppose that $D$ contains a unique cone of the form $\rho : \Delta_{[k]}(\tau) \Rightarrow \theta$. For every index $i \in [k]$, the object $\theta(i)$ in $\text{Seg}(\Omega)$ is irreducible for $(\Omega, D, X)$.

Proof. By definition of a chromology (section 2.9), the arrow $\rho_i : \tau \rightarrow \theta(i)$ is an arrow in a category of quasi-homologous segments (see Definition 2.9). By Lemma 2.14, this means that this arrow is the only arrow of type $\tau \rightarrow \theta(i)$ in $\text{Seg}(\Omega)$. By Remark 4.49, this means that for every arrow $\tau \rightarrow \theta(i)$ in $\text{Seg}(\Omega)$, its image $X(\tau) \rightarrow X(\theta(i))$ coequalizes the pair $GX(\rho) \rightrightarrows X(\tau)$.

Since $\rho$ is the only cone of $D$, this means that the image of every arrow $\nu : \theta(i) \rightarrow \nu$ in $\text{Seg}(\Omega)$ via the functor $X : \text{Seg}(\Omega) \rightarrow \text{Set}$ coequalizes the pair $GX(\rho') \rightrightarrows X(\nu)$ for every cone $\rho' : \Delta_{[k']}(\nu) \Rightarrow \theta'$ in $D$. This shows the irreducibly of $\theta(i)$. □

Proposition 4.52. Let $(\Omega, D)$ be a recombination chromology and $X$ be a functor $\text{Seg}(\Omega) \rightarrow \text{Icm}$. For every irreducible object $\tau$ in $\text{Seg}(\Omega)$, the coequalizer map $q_X : X(\tau) \rightarrow DX(\tau)$ (Convention 4.42) associated with the recombination monoid over $X$ (Definition 4.41) is an isomorphism.

Proof. By Definition 4.48 and universality of coequalizer (4.10). □

Definition 4.53 (Recombination scheme). A recombination scheme is a triple $(\Omega, D, X)$ where $(\Omega, D)$ is a recombination chromology and $X$ is a functor $\text{Seg}(\Omega) \rightarrow \text{Icm}$ such that for every cone $\rho : \Delta_{A}(\tau) \Rightarrow \theta$ in $D$ and object $i \in [k]$, the object $\theta(i)$ is irreducible for $(\Omega, D, X)$.

The following theorem shows that the recombination monoid associated with a recombination scheme is a $W^{\text{mon}}$-pedigrad.

Theorem 4.54. Let $(\Omega, D, X)$ be a recombination scheme. For every cone $\rho : \Delta_{A}(\tau) \Rightarrow \theta$ in $D$, the canonical arrow $i : DX(\tau) \rightarrow \prod_{i \in [k]} DX(\theta(i))$ is a monomorphism in $\text{Icm}$.

Proof. By Definition 4.38, the pullback of two copies of the canonical arrow $X[\rho]$ (see Convention 4.37) is the recombination congruence $G(X, \rho) \rightrightarrows X(\tau)$. If we denote by $p_1, p_2 : P \rightrightarrows DX(\tau)$
the pullback of two copies of the arrow \( \iota \) (see statement), the naturality of the coequalizer map \( q_X : X \to DX \) gives us an arrow \( \lambda : X(\rho) \to P \) making the following diagram commute.

\[
\begin{array}{c}
\xymatrix{
X(\tau) & G(X, \rho) \ar[ll]_{prj_1} \ar[r]^{prj_2} & q_X \ar[d] & P \ar[l]\ar[d]^{p_1} \ar[l]_{p_2} \\
X[\rho] & X(\tau) \ar[l] \ar[d] & DX(\tau) \ar[l]_{\iota} \ar[d] & DX(\tau) \ar[l]_{\iota} \\
\prod_{i \in [k]} X(\theta(i)) & \ar[l]_{\prod_i q_X} \ar[l]_{\iota} \ar[l]_{\iota} \ar[l]_{\iota} \ar[l]_{\iota} \\
}
\end{array}
\]

(4.13)

Let us show that \( \lambda \) is an epimorphism in \( \text{Icm} \) by showing it is orthogonal with respect to the Boolean ic-monoid \( B_2 \) (see Proposition 4.24). First, because \((\Omega, D, X)\) is a recombination scheme, Proposition 4.52 implies that the bottom front arrow of diagram (4.13) is an isomorphism. Second, because \( q_X : X(\tau) \to DX(\tau) \) is a coequalizer map, it is orthogonal with respect to the Boolean ic-monoid \( B_2 \) (Remark 4.31). These two facts imply that, for every arrow \( x : B_2 \to P \), the composite arrows \( p_1 \circ x : B_2 \to DX(\tau) \) and \( p_2 \circ x : B_2 \to DX(\tau) \) admit lifts \( h_1 : B_2 \to X(\tau) \) and \( h_2 : B_2 \to X(\tau) \) along \( q_X \) that make the following diagram commute.

\[
\begin{array}{c}
\xymatrix{
B_2 & X(\tau) \ar[l]_{h_1} \ar[d]_{h_2} \\
X(\tau) \ar[r]_{X[\rho]} & \prod_{i \in [k]} X(\theta(i)) \ar[l]_{\iota} \\
}
\end{array}
\]

Since \( G(X, \rho) \) is the pullback of \( X[\rho] \) along itself, the previous diagram provides an arrow \( h : B_2 \to G(X, \rho) \) for which the equation \( \lambda \circ h = x \) holds. In other words, the arrow \( \lambda \) is orthogonal to the Boolean ic-monoid \( B_2 \) and is hence an epimorphism by Proposition 4.24.

Now, because the equation \( q_X \circ prj_1 = q_X \circ prj_2 \) holds by definition of \( q_X \) and because we showed that \( \lambda \) is an epimorphism, the two arrows \( p_1, p_2 : P \cong DX(\tau) \) must be equal (see diagram (4.13)). Because this pair of arrows is also the pullback of two copies of \( \iota \), the arrow \( \iota \) is a monomorphism (Proposition 4.20).

The following result explains, in abstract terms, why Corollary 4.56 (our main result) holds.

**Theorem 4.55.** Let \((\Omega, D)\) be a chronology and \( X : \text{Seg}(\Omega) \to \text{Icm} \) be a \( \text{W}^\text{mon}-\text{pedigrad}. \)

For every morphism \( f : Y \Rightarrow X \) in \([\text{Seg}(\Omega), \text{Icm}]\), the coequalizer \( Y_X : \text{Seg}(\Omega) \to \text{Icm} \) of the pullback pair of \( f \) along itself is a \( \text{W}^\text{mon}-\text{pedigrad} \) for \((\Omega, D)\) (see the diagrams below).

\[
\begin{array}{c}
\xymatrix{
R & Y \ar[d]_{u_2} \ar[l]^{u_1} & Y \ar[d]_{f} \\
Y & X \ar[l]_{\Rightarrow} \\
}
\end{array}
\]

Proof. By definition, the morphism \( f : Y \Rightarrow X \) coequalizes the pair \((u_1, u_2)\) so that there exists a unique morphism \( f' : Y_X \Rightarrow X \) in \([\text{Seg}(\Omega), \text{Icm}]\) making the diagram given below, on the left,
Now, for every cone \( \rho : \Delta_A(\tau) \Rightarrow \theta \) in \( D \), we want to show that the canonical arrow \( Y_X(\tau) \to \lim_A Y_X \circ \theta \) is a monomorphism. First, notice that the morphism \( f' : Y_X \Rightarrow X \) gives us the commutative diagram given above, on the right, whose the vertical arrows are the obvious one. Since the arrow \( X(\tau) \to \lim_A Y_X \circ \theta \) is a monomorphism by assumption on \( X \) (i.e. it is a \( \mathcal{W}^{\text{mon}} \)-pedigrad), the universal property of monomorphisms (section 4.5) implies that if the arrow \( f'_\tau : Y_X(\tau) \to X(\tau) \) is a monomorphism, then so is \( Y_X(\tau) \to \lim_A Y_X \circ \theta \).

To show that the arrow \( f'_\tau : Y_X(\tau) \to X(\tau) \) is a monomorphism in \( \text{Icm} \), we want to show that it is a \( B_2 \)-monomorphism and use Proposition 4.22. Let \( a, b : B_2 \Rightarrow Y_X(\tau) \) be two arrows in \( \text{Icm} \) for which the equation \( f'_\tau \circ a = f'_\tau \circ b \) holds. First, by Remark 4.31, the coequalizer \( q_r : Y(\tau) \Rightarrow Y_X(\tau) \) is orthogonal with respect to \( B_2 \). Thus, the arrows \( a \) and \( b \) admits lifts \( a' : B_2 \to Y(\tau) \) and \( b' : B_2 \to Y(\tau) \) along \( q_r \), respectively. By assumption on \( a \) and \( b \), the following series of identities holds.

\[
f_\tau \circ a' = f'_\tau \circ q_r \circ a' = f'_\tau \circ a = f'_\tau \circ q_r \circ b' = f_\tau \circ b'
\]

Since the ic-monoid \( R(\tau) \) (see the statement) is the pullback of \( f_\tau \) along itself, the previous series of identities implies that there is a canonical map \( h : B_2 \to R(\tau) \) making the following diagrams commute.

\[
\begin{array}{ccc}
B_2 & \xrightarrow{a'} & Y(\tau) \\
\downarrow{h} & & \downarrow{u_{1r}} \\
R(\tau) & & \\
\end{array}
\quad
\begin{array}{ccc}
B_2 & \xrightarrow{b'} & Y(\tau) \\
\downarrow{h} & & \downarrow{u_{2r}} \\
R(\tau) & & \\
\end{array}
\]

Post-composing the previous diagram with the coequalizer \( q_r : Y(\tau) \to Y_X(\tau) \) of \( u_{1r} \) and \( u_{2r} \) then provides the following identities.

\[
a = q_r \circ a' = q_r \circ u_{1r} \circ h = q_r \circ u_{2r} \circ h = q_r \circ b' = b
\]

This shows that \( f'_\tau : Y_X(\tau) \to X(\tau) \) is a \( B_2 \)-monomorphism and hence a monomorphism by Proposition 4.22. \( \square \)

**Corollary 4.56.** Let \( (E, \varepsilon) \) be a pointed set, \( (\Omega, D) \) be a recombination chromology \( (\Omega, D) \) and \( b \) be an element in \( \Omega \) for which \( (\Omega, D, E^c_b) \) is a recombination scheme. For any sequence alignment \( (\iota, T, \sigma) \) over \( 2E^c_b \), the functor \( D_ET \) of Remark 4.44 is a \( \mathcal{W}^{\text{mon}} \)-pedigrad for \( (\Omega, D) \).

**Proof.** First, by Remark 4.44, the object \( D_ET \) is the coequalizer of the pullback pair resulting from the pullback of the morphism \( \text{rec} : \text{Flan}_T \Rightarrow DFE^c_b \) along itself. Then, by Theorem 4.54, the codomain of \( \text{rec} \) is a \( \mathcal{W}^{\text{mon}} \)-pedigrad for \( (\Omega, D) \). These two facts together with Theorem 4.55 imply that \( D_ET \) is a \( \mathcal{W}^{\text{mon}} \)-pedigrad for \( (\Omega, D) \). \( \square \)

**5. Solving our problem and studying phenotypes**

The goal of the present section is to explain how the formalism developed in the previous sections can be used as a guideline to study the relationship between genotypes, phenotypes and haplotypes. Let \( (\Omega, \preceq) \) be a pre-ordered set, \( (\Omega, D) \) be a recombination chromology, \( b \) be an element of \( \Omega \), \( (E, \varepsilon) \) be a pointed set, \( (\iota, T, \sigma) \) be a sequence alignment over \( 2E^c_b \) and \( \varphi : T \Rightarrow UF\Delta S \circ \iota \) be a phenotypic expression for \( (\iota, T, \sigma) \).
5.1. Predicting phenotypes. Let us explain how, for every cone $\rho : \Delta_{[k]}(\tau) \Rightarrow \theta$ in $D$, the following sequence of arrows, constructed in Remark 4.44, can be used to predict phenotypes.

$$\text{Observation} \quad \text{Haplotypes}^* \quad \text{Haplotypes}$$

$$F\text{Lan}_iT(\tau) \xrightarrow{r_r} D_E T(\tau) \xrightarrow{D_E T[\rho]} \prod_{i \in [k]} D_E T \theta(i)$$

We shall use the same notations as those used in Remark 4.44. First, in the same fashion as in the proof of Theorem 4.55, we can use the universal property of coequalizers to show that there is a canonical morphism of pedigrads $\text{rec} : D_E T \Rightarrow DFE^e_b$ (see section 2.12).

$$R_D \xrightarrow{y_1} \text{Lan}_iT \xrightarrow{\text{rec}} DFE^e_b$$

We can use the morphism $q_{FE^e_b} \circ \text{fml} : F^2E^e_b \Rightarrow DFE^e_b$ (see Remark 4.44) and the canonical arrow $F^2E^e_b(\tau) \to \prod_{i \in [k]} F^2E^e_b \theta(i)$ to form the following diagram in $\text{icm}$.

$$(5.1) \quad \begin{array}{ccc}
F^2E^e_b(\tau) & \downarrow & \\
\prod_{i \in [k]} F^2E^e_b \theta(i) & \downarrow & \\
F\text{Lan}_iT(\tau) & \xrightarrow{r_r} D_E T(\tau) & \xrightarrow{D_E T[\rho]} \prod_{i \in [k]} D_E T \theta(i) & \xrightarrow{\prod_{i \in [k]} \text{rec}' \theta(i)} \\
\end{array}$$

By Definition 4.32, the elements of $F^2E^e_b(\tau)$ can be seen as haplogroups. Thus, for a given haplogroup $h$ in $F^2E^e_b(\tau)$, being able to predict the phenotype of $h$ amounts to being able to lift the image of the element $h$ via the vertical arrow $F^2E^e_b(\tau) \to \prod_{i \in [k]} DFE^e_b \theta(i)$ of the previous diagram along the three horizontal ones.

- **1st lifting step:** the existence of a lift along the rightmost horizontal arrow would mean that one is querying within the right gene pool.
- **2nd lifting step:** the existence of a lift along the middle horizontal arrow would mean that one has enough data for a possible prediction. If the object $D_E T$ is a $\mathcal{W}^{\text{mon}}$-pedigrad for $(\Omega, D)$, then the lift is unique and the haplotype classification is deterministic.
- **3rd lifting step:** a lift along the leftmost arrow always exists as the coequalizer $r_r : F\text{Lan}_iT(\tau) \to D_E T(\tau)$ is an epimorphism (see Remark 4.31). However, the different pieces of information given by the images of the lifts through the phenotypic expression $\mu F\varphi^*_r : F\text{Lan}_iT(\tau) \to FS$ may push one to re-analyze the set $S$ of phenotypes.

**Example 5.1** (Predicting phenotypes). In this example, we illustrate the different types of lifting step explained earlier for diagram (5.1) in the case of our main example (section 2.1). We shall start our discussion as if we had finished discussion Example 4.45. As usual, we will consider the sequence alignment $(\iota, T, \sigma)$ constructed in Example 3.10. We will also take $\rho : \Delta_A(\tau) \Rightarrow \theta$ to be the cone of the same name defined in Example 4.39, which we recall below.

$$\begin{array}{c}
(\bullet\bullet\bullet\bullet)(\circ\circ\circ\circ\circ)(\circ\circ\circ\circ\circ) \quad \theta(a_1) \\
(\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet)(\bullet\bullet\bullet\bullet) \quad \theta(a_2) \\
(\circ\circ\circ\circ\circ)(\bullet\bullet\bullet\bullet)(\circ\circ\circ\circ\circ) \quad \theta(a_3)
\end{array}$$
First, if we take \( z \) to be the element of the set \( F^2E^i_b(\tau) \) displayed below, on the left, then its image through the vertical arrow of (5.1) is given on the right.

\[
\begin{align*}
z &= \begin{pmatrix} \text{ATCATT} \rangle \langle \text{AGCTAC} \rangle \langle \text{CTATAC} \rangle \\ \text{ATCATT} \rangle \langle \text{AGCTAC} \rangle \langle \text{ATATGC} \rangle \end{pmatrix} & \mapsto & \begin{pmatrix} \text{ATCATT} + \text{ATCATT} \\ \text{AGCTAC} + \text{ATATGC} \end{pmatrix}
\end{align*}
\]

Unfortunately, by definition of \((\iota, T, \sigma)\), the tuple given above, on the right, is not in the image of the arrow \( \prod_{i \in [k]} D_{E^i} \theta(i) \to \prod_{i \in [k]} D_{E^i} \theta(i) \) because none of the alleles of \( a, b, c \) or those of their progeny start with the sequences ATCATT and ATCCTAC (see the two sequences given at the top of the image of \( z \)). Thus, the first lifting step cannot be carried out.

If we now take \( z \) to be the element of the set \( F^2E^i_b(\tau) \) displayed below, on the left, then its image through the vertical arrow of (5.1) is given on the right.

\[
\begin{align*}
z &= \begin{pmatrix} \text{AACATT} \rangle \langle \text{AGCTTC} \rangle \langle \text{GTATGC} \rangle \\ \text{AGCATT} \rangle \langle \text{AGCTTC} \rangle \langle \text{ATATTC} \rangle \end{pmatrix} & \mapsto & \begin{pmatrix} \text{AACATT} + \text{AGCATT} \\ \text{AGCTTC} + \text{AGATTTC} \\ \text{GTATGC} + \text{ATATTC} \end{pmatrix}
\end{align*}
\]

Even though each patch contained in the image of the element \( z \) is a patch coming from the alleles of the elements \( a, b, c \), an exhaustive search shows that there is no sum of elements of \( T \) whose image through the map \( D_{E^i} \theta : D_{E^i} \tau \to \prod_{i \in [k]} D_{E^i} \theta(i) \) is equal to the tuple given above, on the right. Thus, even though the image of \( z \) lifts along the rightmost horizontal arrow of (5.1), it does not lift along the middle one.

Finally, take \( z \) to be the \( \rho \)-haplogroup of the set \( F^2E^i_b(\tau) \) displayed below. In this case, the lifting process can be seen as a query about the possible phenotypes that the progeny of two \( \rho \)-genotypes of \( z \) may possess.

\[
\begin{align*}
z &= \begin{pmatrix} \text{ACCACCT} \rangle \langle \text{AGCTTC} \rangle \langle \text{GTATGC} \rangle \\ \text{ACCACCT} \rangle \langle \text{AGCTTC} \rangle \langle \text{ATATTC} \rangle \end{pmatrix} & \mapsto & \begin{pmatrix} \text{ACCACCT} + \text{ACCACCT} + \text{AACATT} \\ \text{AGCTTC} + \text{AGATTTC} + \text{AGCACT} \\ \text{GTATGC} + \text{CTATTC} + \text{TTATAC} + \text{ATATTC} \end{pmatrix}
\end{align*}
\]

Note that each of the \( \rho \)-genotypes making \( z \) are not elements of the functor \( T \) – we are therefore about to make a prediction. Now, the image of \( z \) through the vertical arrow of (5.1) is as follows.

\[
\begin{align*}
\begin{pmatrix} \text{AGCTAC} + \text{ATCATT} \\ \text{AGCTAC} + \text{CTATAC} + \text{ATATGC} \end{pmatrix}
\end{align*}
\]

We can check that the images of the elements \( b + c \) and \( p_4 + p_6 \) of \( F\text{Lan}_i T(\tau) \) through the three horizontal arrows of diagram (5.1) are equal to the previous tuple (for instance, see Example 4.50). These two lifts along the arrow \( F\text{Lan}_i T(\tau) \to \prod_{i \in [k]} D_{E^i} \theta(i) \) give two different phenotypes. Indeed, the image of the element \( b + c \) through the phenotypic expression is \textit{hea} + \textit{dis} while the image of the element \( p_4 + p_6 \) through the phenotypic expression is \textit{hea}. Thus, we can predict that the progeny of the \( \rho \)-haplogroup \( z \) may contain certain diseased individuals, but the variation causing the disease may be recessive in certain cases (as in the case of \( p_4 + p_6 \), which is mapped to \textit{hea}). To understand when the recessiveness of the disease occur, one may want to further refine the phenotypic expression by considering a different set of phenotype \( S \) as well as a different pre-ordered set \( \Omega \).

In conclusion, we see that each arrow of diagram (5.1) provides a qualitative information about the prediction one is trying to make and guide ones regarding the procedure to follow if the lifts fail to exist or fail to give a suitable answer.

5.2. Multiphenotype Mendelian randomization. Let us explain how the phenotypic expression of \((\iota, T, \sigma)\) can be used with the coequalizer \( r : F\text{Lan}_i T \Rightarrow D_{E^i} \) to assess the quality.
of the phenotypic expression itself. First, let us form the pullback of the adjoint arrow of the phenotypic expression in \( \text{Icm} \) along itself, as shown below, on the left.

\[
\begin{array}{c}
\xymatrix{
M_S^2 \ar[r]^{u_1} & F\text{Lan}_1 T \\
& \\ \text{Lan}_1 T \ar[r]_{\mu F \varphi^*} & F \Delta S
} & \xymatrix{
M_S^2 \ar[r]^{u_1} & F\text{Lan}_1 T \\
& \\ \text{Lan}_1 T \ar[r]_{\mu F \varphi^*} & D_E T
}
\end{array}
\]

For every segment \( \tau \) in \( \text{Seg}(\Omega) \), the pullback pair \( u_1, u_2 : M_S^2(\tau) \Rightarrow F\text{Lan}_1 T(\tau) \) can be shown to be a groupoid (where \( M_S^2(\tau) \) is the set of arrows, \( F\text{Lan}_1 T(\tau) \) is the set of objects and \( u_1 \) and \( u_2 \) are the source and target operations). We can then use this groupoid to see if the fibers of the epimorphism \( r_\tau : F\text{Lan}_1 T(\tau) \rightarrow D_E T(\tau) \) are made of single connected components.

If a fiber of \( r_\tau^{-1}(y) \) happens to be a single connected component, then the haplotype \( y \) in \( D_E T(\tau) \) can be associated with a unique phenotype. If the fiber of \( r_\tau^{-1}(y) \) is made of several connected components, then the haplotype \( y \) may involve markers whose dominance relationship may be intricate. A better analysis of the properties of the groupoid \( u_1, u_2 : M_S^2(\tau) \Rightarrow F\text{Lan}_1 T(\tau) \) may then be needed to better understand the kind of phenotype with which the haplotype \( y \) can be associated. This could mean a redefinition of the phenotypic expression itself along with the use of a different pre-ordered set \( \Omega \) whose colors could be used to encode the various external factors that may cause the disconnectedness of the fibers; for more insight on this problem, see [21, Multiphenotype Mendelian randomization].

**Example 5.2** (Disconnected phenotypes). In the case of our main example, presented in section 2.1, we showed, in Example 4.45, that the two elements \( b+c \) and \( p_4+p_6 \) of \( F\text{Lan}_1 T(\tau) \) (where \( \tau \) is the peak of the cone \( \rho \) displayed in Example 5.1) belonged to the same fiber of \( r_\tau : F\text{Lan}_1 T(\tau) \rightarrow D_E T(\tau) \), namely the fiber of the element of \( D_E T(\tau) \) represented by the following equation.

\[
b+c = p_4 + p_6
\]

Then, in Example 5.1, we showed that the two elements \( b+c \) and \( p_4+p_6 \) of \( F\text{Lan}_1 T(\tau) \) actually belonged to two different connected components of the groupoid structure of \( u_1, u_2 : M_S^2(\tau) \Rightarrow F\text{Lan}_1 T(\tau) \), namely \( b+c \) belonged to the connected component classifying the phenotype \( \text{hea} + \text{dis} \) while \( p_4+p_6 \) belonged to the connected component classifying the phenotype \( \text{hea} \).

Here, the two phenotypes \( \text{hea} + \text{dis} \) and \( \text{hea} \), even though different, are related by an implicit order relation \( \text{hea} \leq \text{hea} + \text{dis} \) reminiscent of the dominance relationship mentioned in Example 5.1. At a more general level, this type of relation could be used to refine the groupoid structure into a category whose arrows \( \varepsilon : g_1 \rightarrow g_2 \), on pairs of elements \( g_1 \) and \( g_2 \) in \( F\text{Lan}_1 T(\tau) \), would be given by equations of the form \( \mu F \varphi^*(x_1) + \varepsilon = \mu F \varphi^*(x_1) \). Here, we would have an arrow \( \text{dis} : p_4 + p_6 \rightarrow b + c \). The concept of intermediate phenotype [21] could then be encoded by expressing certain phenotypes in terms of other phenotypes. These equations would lead to relations between the arrows, which could be translated in terms of ‘arrows between arrows’. In fact, through the process of what is called a resolution [12], we could generate a higher category that could be used to study the complex causal relationships occurring between phenotypes from a genotypic and predictive point of view.

6. Conclusion

Pedigrafs in the category of idempotent commutative monoids were shown to provide a framework in which it is possible to talk about recombination events, haplotypes and genetic linkage. In section 4.4, we showed how the concept of sequence alignment could be used to link genotype to phenotype via a span structure in the category of idempotent commutative monoids (see Remark 4.18). In Example 4.19, we showed how this span structure could be used...
with coequalizers and the concept of monomorphism to localize the variations responsible for a phenotype. Finally, in the last part of the paper, from section 4.7 to section 5.1, we showed how one can use this span structure to predict the phenotype of a genotype that is not part of our dataset.

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