Categorical hierarchical models for cell systems?

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Abstract

The aim is to explain and explore some of the current ideas from category theory that enable various mathematical descriptions of hierarchical structures.

Introduction

This chapter seeks to explore some of the current ideas that provide abstract models for hierarchical systems in general and cell systems in particular. The models are based on category theory and as that theory is to a large extent relatively unknown to workers in (mathematical and computational) biology, the chapter will have to introduce some of the elementary language and concepts of that theory. We will attempt to do this through fairly 'common or garden' mathematical situations which themselves have aspects of hierarchical structures about them. Our aim is to present enough of the ideas to make it possible for the enterprising reader to start delving further into the way in which others (Rosen, [20], Ehresmann and Vanbremersch, see for instance, [8]) have seen category theory as a potentially useful language and toolkit of concepts for use in this area.

Discrete or network models for complex systems are commonplace in the literature. Such models can be enriched using simple concepts from category theory. Essentially the additional feature is to consider not just links between 'nodes' but also sequences of 'composable' such links. This adds just enough algebraic structure into the combinatorial network model to allow a whole range of useful new ideas to become available. Certain features can be investigated using a 'toy model' which does not assume anything more than basic arithmetic, yet shows up some of the hidden assumptions in more complex models. Of course a 'toy model' can not reveal deep structure, it is little more than a thought experiment, so our aims are deliberately limited.

1 Category Theory : History and Motivation.

The first paper in category theory was by Eilenberg and Mac Lane in 1945 [9]. It aimed initially to describe (i) interaction and comparison within a given context (Topological spaces, Groups, other algebraic structures, etc.) and (ii) interactions between different contexts, for instance within the area of pure mathematics known as algebraic topology, problems in the theory of spaces are attacked by assigning various types of algebraic gadgetry to spaces, thus translating the topological problem to a, hopefully more tractable, algebraic one. A category consists of objects and 'morphisms' between them, thought of as 'structure preserving mappings'.

Even as early as the 1950s and 1960s, category theory had become a highly successful language providing general tools for revealing common structure between different contexts. New

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concepts (limits, colimits, products, coproducts, etc.) were defined abstractly and these definitions highlighted the properties that had been there in the examples but had often been hidden by context specific details. Already in 1958 Rosen had tried using elementary categorical language to help with the modelling of biological systems. In the 1960s, Lawvere's thesis and other related work by Benabou and others at about the same time, shed new light on what it meant for a structure to be 'algebraic'. This linked up with the semantics of formal languages and thus with logic. Lambek and Lawvere (1968-1970s) showed that there was an interpretation of the typed λ-calculus, which was a rich model for some aspects of the logical theory of sets, within category theory. Here formulae are interpreted as the objects, and proofs as the morphisms. (For us one important point is that the morphisms are no longer structure preserving 'mappings', they are just 'morphisms'!) This gave:

a) Models for Set theory, but something much richer is true, the 'sets' are 'variable sets'; and they can be applied in many more contexts and have their own internal categorical logic, and

b) links to the newly emerging discipline of Theoretical Computer Science. (For instance the semantics of programming languages has been greatly enriched by the work of Lambek and Scott on Cartesian Closed Categories,[15], Scott, Plotkin and Smyth on Domain Theory, using categorical and topological insights, and Arbib and Manes [1] using partially additive categories.)

More recently Girard (1987) has introduced Linear Logic. This is a 'resource sensitive logic' or 'logic of actions' and is, once again, firmly based on a categorical semantics. The correspondence here is more nearly 'Formulas' with 'States', and 'Proofs' with 'Transitions'. Within Control Engineering for some time a network model (Petri nets) had been used as an analytic tool for developing concurrent control systems. In 1991, Meseguer and Montanari linked Petri nets, and thus concurrency, with models of Linear Logic. This linked 'States' with 'Objects' and 'Transitions' with 'Morphisms'. This work of Meseguer led onto work on a rewriting language, MAUDE, providing a semantics of object systems and so a 'logical theory of concurrent objects' [16]. (The links of this work with the modelling of biological systems is briefly explored in [10].)

For us these developments present the seductive suggestion that by adapting and extending some hypothetical model of (part of) a cell system one might get not only a model but also some corresponding logical framework, possibly even a rich programming language based on that logical language. That is a long way in the future. Suffice it to say that Petri nets are also widely used in modelling manufacturing systems, and they exist in fuzzy, stochastic and timed variants, but as yet no categorical description exists for these rich variants. Can one hope for a Petri net/ Linear Logic like description of some of the metabolic systems in the body? Who knows?

With these hints of what might be possible in our wildest dreams, let us summarise some of the characteristics of a formal language in a categorical context. (i) It will be many sorted with a collection of states/ objects. (ii) Between the states there will be transitions or morphisms that may be thought of a 'proofs'. The constructions within the logic will give us new constructions of objects from collections of old ones, so we might have a category with some extra structure - but what structure?

2 Categorical models for hierarchical systems.

Later we will be looking at some aspects of the theory of hierarchical systems as developed by Ehresmann and Vanbremersch (1985 to the present), but to start with we should examine the motivation for such a theory. The idea is that a categorical formal language, that is rich enough to describe and allow analysis of aspects of complex hierarchical systems, should be applicable to cell systems and to other situations such as manufacturing systems. We should start with a categorical model of a hierarchical system and analyse its logical structure both for its own sake and from the modelling aspect (is the model robust enough to experimental situations?)

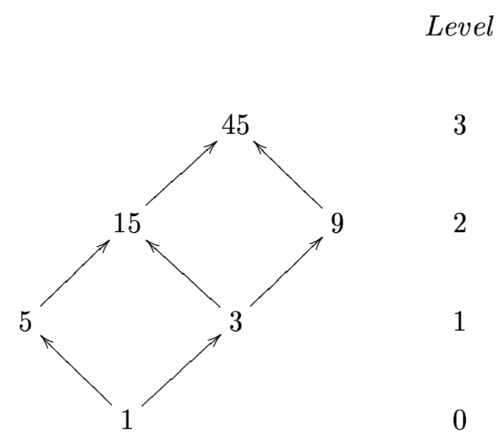
Simple Illustrative Example of a Hierarchical System assuming very little mathematical background.

The divisors of 45 form, in the first instance, a set

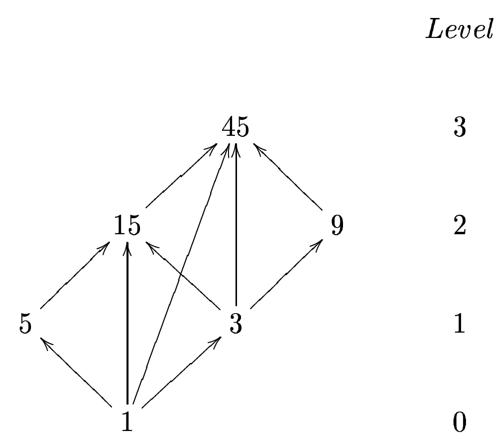
$$Div(45) = \{1, 3, 5, 9, 15, 45\}$$

Of course there are relationships between the elements : i is related to j if i exactly divides j:

Diagram of the structure:



This is an example of a partially ordered set. N.B. only the essential 'generating' arrows are shown here. If we include the 'composite' arrows, we get a more complicated diagram.



together with a loop at each vertex since for any i, i exactly divides itself! Each level of the 'hierarchy' measures in some sense the 'complexity' of the objects at that level.

In going from simple diagram of the partially ordered set (poset) to that including the composite arrows we are starting the transition from posets to categories. What is a category in this sense?

A *category* consists of

- a collection of *objects* $C = \{i, j, k, \dots, \text{ etc.}\}$;
- collections of *arrows* or *links* or *morphisms* (alternative terms depending on taste, context etc.);
- each arrow has a *source* and *target* and $C(i, j)$ will denote the set of arrows from source i to target j, if $f \in C(i, j)$ we might also write $f : i \to j$ or $i \xrightarrow{f} j$;

- composition of arrows, when this makes sense

$$C(i,j) \times C(j,k) \to C(i,k)$$

$$i \xrightarrow{f} j, \quad j \xrightarrow{g} k \qquad i \xrightarrow{fg} k$$

- identities : for each object i, there is an special 'identity arrow' $1_i \in C(i,i)$

such that

(i) associativity : $(fg)h = f(gh)$ if either makes sense;
(ii) identities: if $f : i \to j$, then $1_i f = f = f 1_j$.

Examples

(Based on $Div(45)$)

1. D_0 Objects – divisors of 45

$$D_0(i,j) = \begin{cases} \text{one element} & \text{if } i \text{ divides } j \\ \text{empty} & \text{otherwise} \end{cases}$$

Composition : - only one choice really!!

Identities : i always divides itself!

In fact any poset $(X, \leqslant)$ gives a category with objects the elements of X, and with

$$X(i,j) = \begin{cases} \text{one element} & \text{if } i \leqslant j \\ \text{empty} & \text{otherwise} \end{cases}$$

(Small) categories generalise partially ordered sets by allowing multiple arrows between objects.

2. D_1 Objects – divisors of 45

$D_1(i,j)$ = set of paths from i to j in the diagram of $Div(45)$.

Thus, for instance,

$$D_1(1,45) = \left\{ \begin{array}{c} 1 \to 5 \to 15 \to 45 \\ 1 \to 3 \to 15 \to 45 \\ 1 \to 3 \to 9 \to 45 \end{array} \right\}$$

Note that all paths (following the arrows) are used and are considered to be distinct. This category D_1 is the *free category* on the Hasse diagram of $Div(45)$. That diagram is a directed graph and given any directed graph, Γ, define

$C := FCat(\Gamma)$

by

Objects $(C) = V(\Gamma)$, the set of nodes or vertices of Γ;

$C(u,v)$ = the set of directed paths in Γ from vertex u to vertex v.

Composition – concatenation of paths;

Identity – 'empty path' at a vertex.

As the notation suggests, this category is called the *free category* on Γ.

3. D_2 will not simply be a category.

In a category, C, each $C(i,j)$ is a set; in an *enriched category*, it will have more structure – in our example, each $D_2(i,j)$ will itself be a category (in fact a poset):

As before,

D_2 Objects – divisors of 45

but

$$D_2(i,j) = \begin{cases} Div(\frac{j}{i}) & \text{if } i \text{ divides } j \\ \text{empty} & \text{otherwise} \end{cases}$$

so for example $D_2(3,45) = Div(15)$ so looks like

$$\begin{tikzcd}
& \cdot & \\
\cdot \arrow[ur] & & \cdot \arrow[ul] \\
& \cdot \arrow[ul] \arrow[ur] \arrow[uu] &
\end{tikzcd}$$

If i, j and k are in D_2, there is an obvious mapping

$$\begin{array}{ccccc} D_2(i,j) & \times & D_2(j,k) & \to & D_2(i,k) \\ a & & b & & ab \end{array}$$

given by the product . of numbers - it preserves the order, it is an 'enriched composition'. D_2 is an 'order enriched' category. (Uses of order enriched categories relevant to the subject matter of this chapter include the book by Arbib and Manes already mentioned [1] and Goguen's book [13] in which a special form there called a $\frac{3}{2}$-category is used to provide structure for sign systems within Algebraic Semiotics.)

Further examples: ('Big' categories)

The generic form of these is:

- All objects with some similar structure;
- All morphisms i.e. mappings that preserve that structure.

Name	Objects	Morphisms/ Arrows
Sets	sets	functions
Posets	partially ordered sets	monotone functions
Spaces	topological spaces	continuous functions
Groups	groups	homomorphisms
Cat	small categories	functors

Colimits

e.g. LCMs

Yes, LCM does equal *least common multiple*, so it is the least of the common multiples. Thus lcm(9,15) = 45, lcm(3,5) = 15, and so on.

We do need a bit more precision, of course. In the natural numbers, 1,2, ... , we say c is a *common multiple* of a and b if c is a *multiple* of a (so there is some d with $c = da$), and c is a multiple of b (so there is some e with $c = eb$). We note that in the diagram for $Div(n)$ for any n, we would have

$$\begin{tikzcd}
& c & \\
a \arrow[ur, bend left] & & b \arrow[ul, bend right]
\end{tikzcd}$$

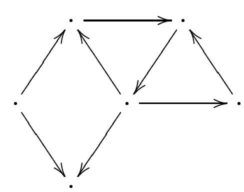
This diagram is a *(co)cone* on the pair a, b. It says c is a *common multiple* of a and b.

Now bring 'least' into play:

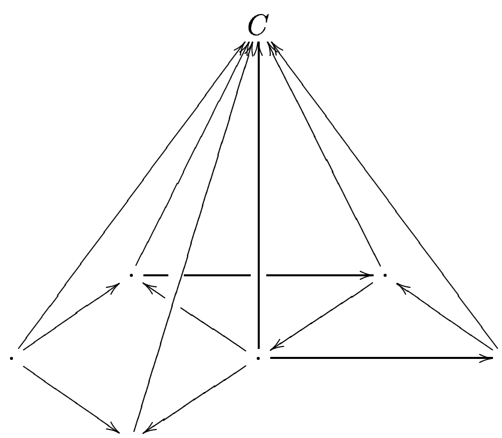
$$
\begin{tikzcd}
 & c & \\
 & \mathrm{lcm}(a,b) \arrow[u] & \\
a \arrow[ur] \arrow[uur, bend left] & & b \arrow[ul] \arrow[uul, bend right]
\end{tikzcd}
$$

This type of situation can be abstracted and generalised to give the notion of 'colimit'. The 'input data' for a colimit is a diagram D, that is a collection of some objects in a category $\mathcal{C}$ and some morphisms between them. The output will be an object Colim$D$ in C. Any (co)cone with base the diagram D and vertex C say. Any such cocone factors through the colimiting cocone:

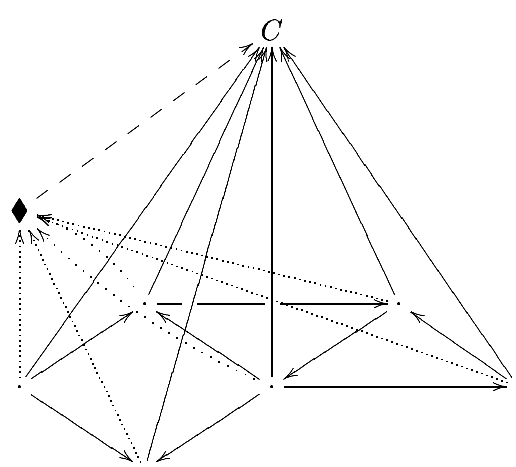
$D =$



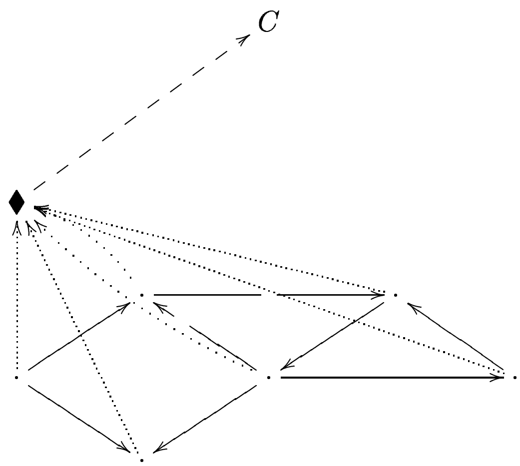
Cocone with base D and vertex C:



The next step is where the colimit sits in this picture as ♦ = colimit D and the dotted arrows represent new morphisms:



and stripping away the 'old' cocone gives the factorisation of the cocone via the colimit:



Intuitions:

From beyond (or above in our diagrams) D, an object 'sees' the diagram D 'mediated' through its colimit, i.e. if it tries to interact with the whole of D, it has to do it via colim D.

Example The lcm is the colimit of the diagram

$$\begin{tikzcd} a & & b \\ & \mathrm{gcd}(a,b) \arrow[ul] \arrow[ur] & \end{tikzcd}$$

The gcd, from a lower level of the hierarchy, 'measures' the interaction of a and b.

Some people have viewed biological organs as colimits of the diagrams of interacting cells within them.

Warning. Often colimits do not exist (in $\mathcal{C}$) for some diagrams. However, one can add colimits in a completion process, i.e. freely for a class of diagrams, and then compare these 'virtual colimits' with any that happen to exist. An example of this process would seem to be the introduction in Neural Net Theory in the 1980s of the notion of 'virtual neurons' or 'assemblages' where an interacting subnet of 'neurons' exhibited behaviour as if it was a (more powerful) single neuron. Perhaps the superstates considered by Bell and Holcombe [3] are similarly 'formal' colimits. Instances of biological situations that lead to diagrams of this sort and hence to colimits occur in the work of of Ehresmann and Vanbremersch, mentioned below in a bit more detail, in Dioguardi [7] where they are used to model 'the hepatone', which is a model of the inter-action of certain major cell types in the liver, and, generically, in the discussion of 'glue' in the study of integrative biology by the second author ([18, 19]).

It is important to note that a colimit has more structure than merely the sum of its individual parts, since it depends on the arrows of the diagram D as well as the objects. Thus the specification for a colimit object of the arrows which define it can be thought of as a 'subdivision' of the colimit object.

Much of this has been leading up to an introduction to the notion of a (categorical model for a) hierarchical system as formulated by Ehresmann and Vanbremersch, [8].

They consider a basic category $\mathbb{H}$ with specified objects and arrows. A partition of $Obj(\mathbb{H})$, the set of objects of $\mathbb{H}$ into $p+1$ classes (*levels*) labelled $0, 1, \ldots, p$ such that each object A' at level $n+1$ (with $n < p$) is the colimit in $\mathbb{H}$ of a diagram A of linked objects at level n.

We refer the reader to the papers of Ehresmann and Vanbremersch and their web page `http://perso.wanadoo.fr/vbm-ehr/`

and also to related pages such as that of Amiguet
`http://iiun.unine.ch/people/mamiguet/index.html`

Queries

(i) Why is A only made up of objects and links at level n? In 'cell systems', does one need *shared* objects of lower levels within the diagram?

(ii) How can one handle computationally, or even mathematically, the properties of A', given knowledge of A?

Parting thoughts

a) To model manufacturing control systems, models such as Petri nets, timed event graphs, etc. exist in numerous flavours, *stochastic*, *fuzzy*, etc. These seem 'enriched versions'. Is there a way of handling hierarchical systems in which these 'enrichments' play a significant role. Some small progress has been made in this direction - but so far it is inconclusive. For a model of computation using enriched categories see [11].

b) *E-V hierarchical systems* try to model cell systems and do consider weighted arrows. Would a variant of their theory, but using (poset or lattice) enriched categories enable an amalgam of their rich conceptual basis with the rich computational machinery already developed from a) above. Would that be useful?

c) Are there 'formal language' aspects of the hierarchical systems, capable of providing models for cell systems?

There is a good practical interpretation of Linear Logic for manufacturing systems (Girault, Thesis: LAAS, Toulouse 1997,[12]) Can such a logic be found for Biological Systems? What should it entail?

d) What might be a feasible successful biological model in the above context? Recall that fractals have been considered successful because they showed that complex variation could result from a very simple model. However, many fractals are very simple, since they are defined by iterated function systems, based on iterates of a single map. Examples need to be develop of the next level of complexity, where also some actual computation, rather than experimentation, is feasible because of the algebraic conditions imposed by the structure of the system. Thus a research programme would be to combine the algebra of rewriting [2], which considers the consequences of rules, with some continuous variation as in fractals, to see how a range of 'colimit structures' can develop. A generalisation of rewriting to categories and to actions of categories is given in [4].

e) We should also note the work of Dampney and Johnson on information systems, [6], which showed that simple commutative diagram considerations could have useful consequences in simplifying a complex system (and so saving money). Since efficiency is of importance for biological systems, we would hope to find examples of analogous considerations.

f) Another potential area for development is that of 'Higher Dimensional Algebra', see the Introduction given in [5]. This shows that one of the contributions of category theory is not only to give a useful general language for describing structures but also, in a self reference mode, that in order to describe the array of structures which have arisen in mathematics new mathematical structures have been found needed, and that these structures have proved of independent interest. Not only that, a crucial step in developing category theory is to have an algebraic operation, composition of arrows, which is defined under a geometric condition, that the source of one arrow is the target of the other. So one is led to envisage more general kinds of compositions. An overall slogan in one aspect of the applications of these more general structures was

Algebraic inverses to subdivision.

That is, we may know how to cut things up, subdivide them, but do we have an adequate algebra which encodes the structure and rules which govern the behaviour of the result of putting them together again? It was found, as is described with references to the literature in [5], that there are forms of what are called multiple categories which do have convenient properties in some situations in this regard. These ideas have led to new mathematics which has enabled new descriptions and new computations not available by other means. The enriched categories to which we referred earlier can also be regarded as forms of multiple categories.

The situation is even more elegant in that we generally think that composition is described mathematically by forms of algebra. There is a growing body of mathematics called 'co-algebra' (see for example [14]) which seems to give a possible language for subdivision. The combination of these two strands of composition and subdivision could well be important for broader applications in the future.

Another theme related to 'algebraic inverses to subdivision' is 'non commutative methods for local-to-global problems'. See [5] for an example of how a two-dimensional structure proposed in 1932 for geometric purposes, and in which the operations were always defined, was found to reduce to a commutative one. It is well known that one aspect of the foundation of quantum mechanics was the introduction of non commutative operations: doing an observation A and then an observation B will not necessarily give the same result as in the other order: in symbols, we may have $AB \neq BA$. Higher dimensional algebra gives almost an *embarasse de richesse* of such non commutative structures, through the use of operations which are defined only under geometric conditions. It is still early days, but intuition suggests that we require a rich form of mathematics, and one in which algebra is partly controlled by geometry, for new descriptions of the richness of complication of life forms.

g) Finally, we mention that the idea of structures evolving over time can be incorporated in categorical models by considering categories varying over time, so that the colimits evolve within the categories. Further, forms of multiple categories have generalised notions of colimits, and so of ways of building a 'structure' out of parts. Again, we can consider adding a time parameter on such a multiple category, so that it and its internal structures are evolving with time.

Conclusion

We hope that pointing out the existence of this categorical mathematics will help the formulation of applications and also suggest ways to new forms of mathematics required for the biological applications.

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