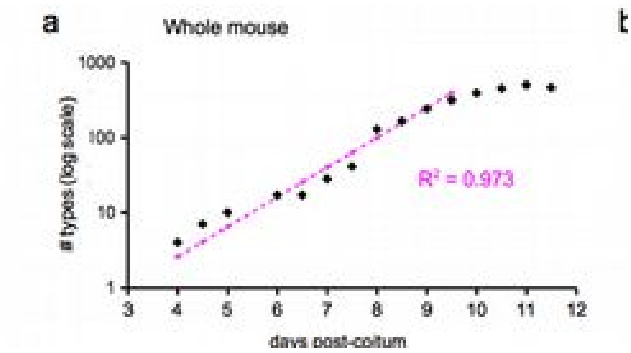
Waites and Measures (2)

I am pleased to say that my collaboration with William Waites, which I described in the blog post *Waites and Measures*, has continued, and has just resulted in the publication of another paper (see links). In this paper, we suggest a solution to a scientific problem that has frustrated me for a very long time.

It is a cliché of developmental biology that organisms increase their complexity as they develop from a relatively featureless egg to an early embryo to a foetus and on to the anatomical richness of the fully-formed, mature body. Nobody comparing the simplicity of an egg or the 'ball of cells' stage of embryonic life with an adult would argue with the general statement that complexity and order has been gained, but it has always been very difficult to quantify this order to make a sweeping statement into something scientifically measurable. Without a measurement of order, one cannot compare the order of different stages of development, or the order achieved by different organisms, or the order achieved (or not) in the case of abnormal development or disease. Nor can one explore, in a specific way, the relationships between creation of order and the demand of energy to create it.

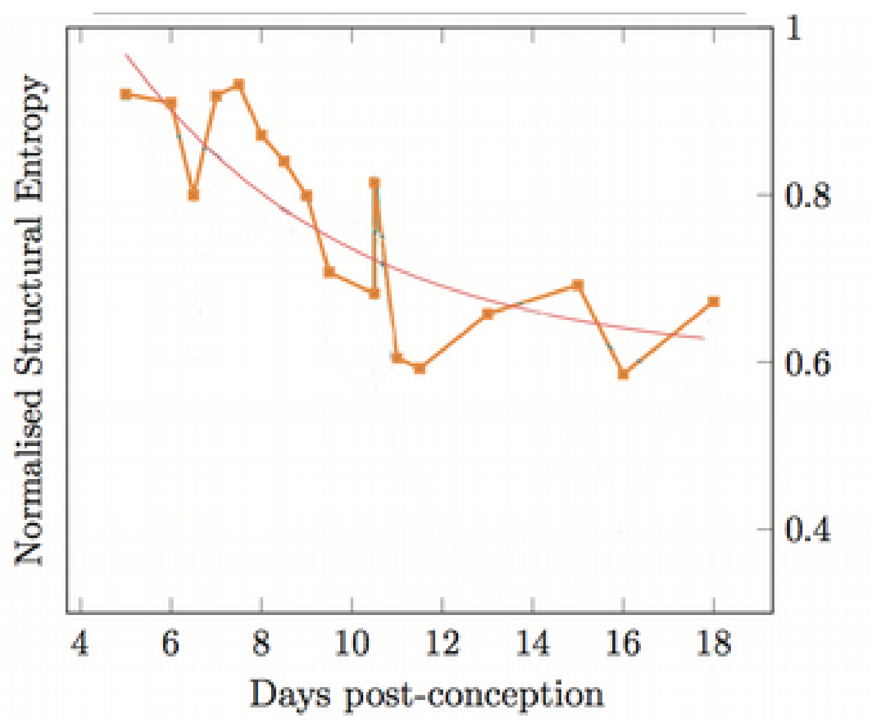
A few years ago, I made a very crude attempt to examine the rising complexity of embryos, in a relative way only, by a method that was very, very crude (arguably cruder that that!). Anatomists who began to study embryonic development centuries ago gave names to all of the structures they saw. My approach was simply to count the number of distinct entities present at every stage of embryogenesis, and plot that number against developmental time (graph right, copied from my 2016 paper – see Links). The outcome was



a embryonic period characterized by a steady exponential growth in the number of distinct tissues, followed by a levelling off in the foetal period. The main interest of the finding was the exponential growth is what one would expect if each generation of complexity depended for its creation on the complexity already achieved in the last. The work was very minor, and published in a then-new journal created specifically as an outlet for pieces of work that are interesting but smaller than that in a conventional paper. It was also very limited – the numbers did not mean anything in absolute terms, and in any case the study relied on a list of entities what was created by humans studying anatomy, rather than being something measured objectively from anatomy itself.

I shared this work with William when we met over coffee, and voiced my frustration that there was not a better measure. He finished his drink and wandered off with a far-away look in his eye. A few days later, he asked to see me again; by then, he had a plan. The plan was to introduce a new measure of anatomical order, which he called Structural Entropy. "Entropy" is a concept associated with disorder in both thermodynamics and in information theory, and the concept in the two fields is related (at deep levels of physics, information has a thermodynamic and energy value; indeed, a colleague of mine calculated that the total information content of the Internet has a mass, by $e=mc^{2}$, of a typical strawberry).

In information theory, entropy is a measure of uncertainty. To measure structural entropy in the embryo, an image of a slide is digitized, and the computer chooses a random pixel in the image, and takes a random walk of n steps across the image. It does this many times, and for each tissue type on which it starts, it measures the probability of landing on each other tissue type after taking n steps. These probabilities, and the total number of tissues present, are then used to construct the measure of structural entropy (mathematical details are in the paper). Doing this for sections of embryos from the Edinburgh Mouse Atlas, at different stages of development, allowed us to gain measurement of structural entropy through time. Plotting this over time resulted in this graph. Overall, there is a pattern of steady decrease of entropy – increase of order – over time. The progression is not completely smooth. The 'blip' around days 7-8



corresponds to gastrulation, an event that involves very significant rearrangement of the embryo's structure. The minimum at 11 days corresponds to the transition between the embryonic period, when the basic structure of the body is set up, and the foetal period in which individual organs form and add internal details.

It is pleasing to see that this measure, obtained automatically by image analysis, does bear out the instinctive idea that embryos become more ordered (entropy drops) with time.

The other pleasing thing about the paper, at least to us, was that the editors did not force us to eradicate all traces of humour (as most do). My favourite was William's explanation about why he used the word 'Entropy' in the title of the new measure; .

When Claude Shannon was discussing with John von Neumann what to call the quantity that came to be known as 'entropy' in Information Theory, the latter famously quipped,

"You should call it entropy, for two reasons. In the first place your uncertainty function has been used in statistical mechanics under that name, so it already has a name. In the second place, and more important, nobody knows what entropy really is, so in a debate you will always have the advantage. (Tribus & McIrvine, 1971)"

If we end up in a conference 'debate' (ie if we ate attacked ferociously in the usual academic manner), we'll try to remember this advice.

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Links

The new paper introducing structural entropy; Waites W, Davies JA (2019) Emergence of structure in mouse embryos: structural entropy morphometry applied to digital models of embryonic anatomy. *J Anat*. 2019 doi: 10.1111/joa.13031.
https://onlinelibrary.wiley.com/doi/full/10.1111/joa.13031

Davies JA (2016) Anatomical complexity is acquired at an exponential rate during mouse embryonic development. *Matters* doi 10.19185/matters.201604000005