INTERVIEW

The people behind the papers – Charlotte Manser and Ruben Perez-Carrasco

Conserved developmental processes often take place at different tempos in different species, but the mechanism underpinning this is not well understood. A new paper in Development presents a novel mathematical framework to explore the molecular basis of developmental timing. To learn more about the story behind the paper, we caught up with first author Charlotte Manser and corresponding author Ruben Perez-Carrasco, group leader at Imperial College London, UK.

Charlotte, how did you come to work in the lab and what drives your research today?
CM: I joined the lab for my PhD starting in 2021. I was looking for a lab which focused on theory in biology, using tools from maths and physics to solve interesting questions, but also keeping its work connected to experiments. I felt that I ‘d learnt a lot of useful techniques from my maths degree for puzzle solving and wanted to use them in a more exploratory field. Ruben’s work fits this brief perfectly! I’m still excited by all the unknowns in biological research. Especially within development, which is so complex because the organism is building itself, so everything is changing all the time, I feel that mathematical techniques are important to unravel the underlying control programmes.

Tell us about the background of the field that inspired your work
RP-C: Recent research from various wet-lab groups has shown that embryos of different species develop at different speeds, yet follow conserved genetic programmes. This discovery has resulted in the hunt for the molecular mechanisms that control these speeds in specific tissues. However, if we want to understand the underlying general principles that allow for this temporal flexibility, we need a quantitative framework that can accommodate these phenomena. This sparked our curiosity and led us to develop a framework based on dynamical system theory, unlocking exciting new possibilities for exploring developmental tempo from a mechanistic perspective.

Embryos of different species develop at different speeds, yet follow conserved genetic programmes

Can you give us the key results of the paper in a paragraph?
CM & RP-C: A crucial aspect of tempo control is maintaining function. We have developed a mathematical method to define function and tempo in a quantitative way by studying the orbits of gene expression: the sequence of molecular expression combinations in specific cellular programmes. Measuring and controlling distances between orbits allows us to identify molecular mechanisms capable of regulating developmental tempo.

When doing the research, did you have any particular result or eureka moment that has stuck with you?
CM: Finding the functions of parameters which can reliably predict the distances between orbits connecting function with molecular mechanism was very nice. It took a lot of time, doing calculations, staring at different plots and having discussions around the blackboard trying to intuit what was happening.

And what about the flipside: any moments of frustration or despair?
CM: It took a while to transform classical tools of dynamical systems that are usually designed for steady states. For instance, pinning down the exact form of prefactor heterogeneity to use. Since the whole second half of the paper depends on that, I was quite stressed when I’d been working for weeks to find the form and it still wasn’t working!

Why did you choose to submit this paper to Development?
CM & RP-C: It is important to us that the paper reaches the right audience. We want it to be read by experimentalists who can put our groundwork to good use. Additionally, Development is not only at the centre of the developmental biology community but also has a track record of supporting the use of mathematical models to understand basic principles of developmental biology, fitting our criteria perfectly.
What is next for you after this paper?
CM: I want to keep exploring the role of tempo in different developmental systems. At the moment, I am working on a new model for the segmentation clock, hoping to shed light on tempo in a way that hasn’t been possible before because of a lack of the temporal framework. I have also started a new collaboration with a group studying differences in corticogenesis speed between species. I am looking forward to applying my theoretical framework introduced in this paper to their single-cell transcriptomics data.

Where will this story take your lab next?
RP-C: In the lab, we are thrilled to explore the temporal aspects of cell decision-making. Some applications, as Charlotte mentions, will remain in developmental biology, but our interests extend beyond that. We are also excited about potential applications in synthetic biology and immunology, where controlling the timing of a particular function within a system is crucial. I find the potential applications of this work really exciting.

Finally, let’s move outside the lab – what do you like to do in your spare time?
CM & RP-C: We’ve started playing Dungeons & Dragons as a lab, with Charlotte as our Dungeon Master and Ruben as a cheese-loving sorcerer (joined by two warlocks, a bard and a cat). Beyond our epic campaigns, we also share a love for music. Charlotte rocks the bass trombone in a brass band, and Ruben plays the clarinet in a woodwind ensemble. Adding to our creative endeavours, we’ve recently launched a sketching club in the Department of Life Sciences at Imperial College London.

Reference