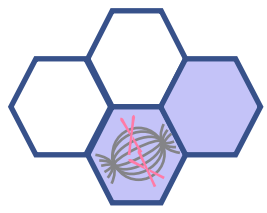


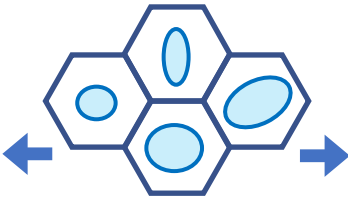
## Introduction

Cells are exposed to mechanical forces in biological tissues which they must respond to maintain tissue homeostasis and physiology. Forces are known to upregulate cell division promoting cell cycle progression and mitotic entry [1,2]. Recent advances have revealed that this could occur through the deformation of the nucleus in response to forces [3]. Forces are transmitted to the nucleus through the linker of the nucleoskeleton and cytoskeleton (LINC) complex [4]. It was proposed that force-induced nuclear deformation promotes the widening of the aperture of the nuclear pore complexes [5]. This in turn, promotes the nuclear translocation of small proteins, namely YAP1 and Cyclin B1 to promote mitotic entry [3, 6]. However, most of these studies subject cells to fast strain rates which do not emulate the slower strain rates commonly seen *in vivo*. Here, we investigate the mechanism underlying nuclear force sensing and how strain rates affect nuclear deformation and cell division.

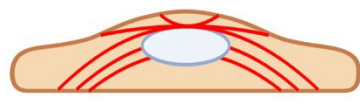
## Aims



How do different strain rates affect the division response?

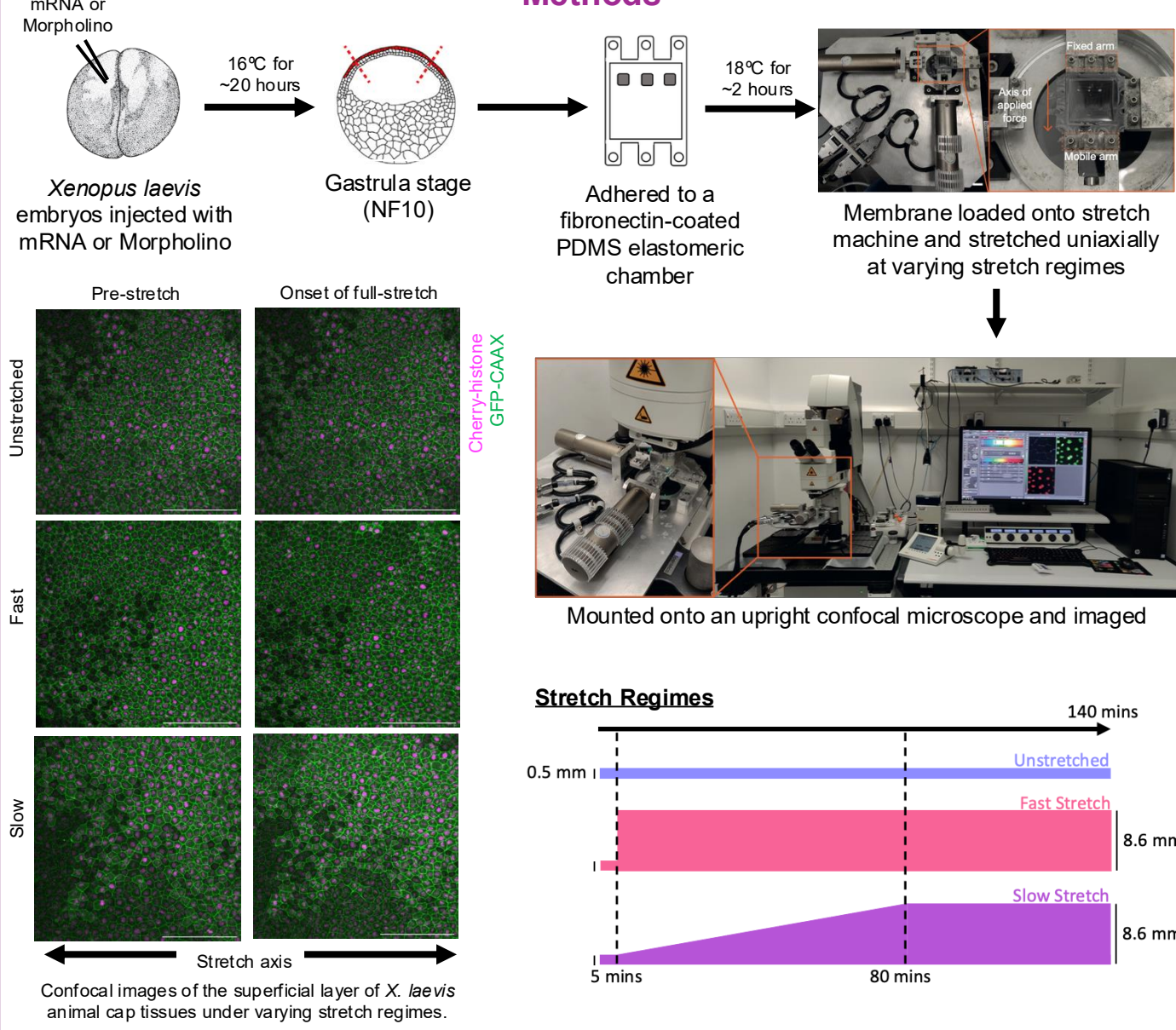


How do different strain rates affect nuclear mechanics?

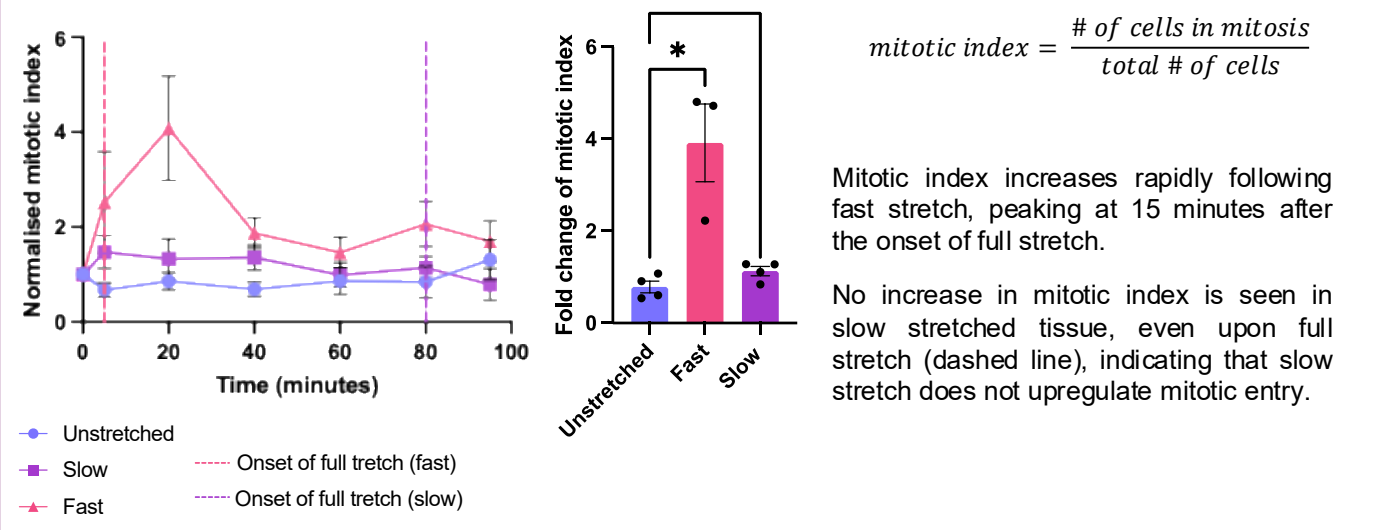


Role of the LINC complex in regulating nuclear deformation in response to stretch?

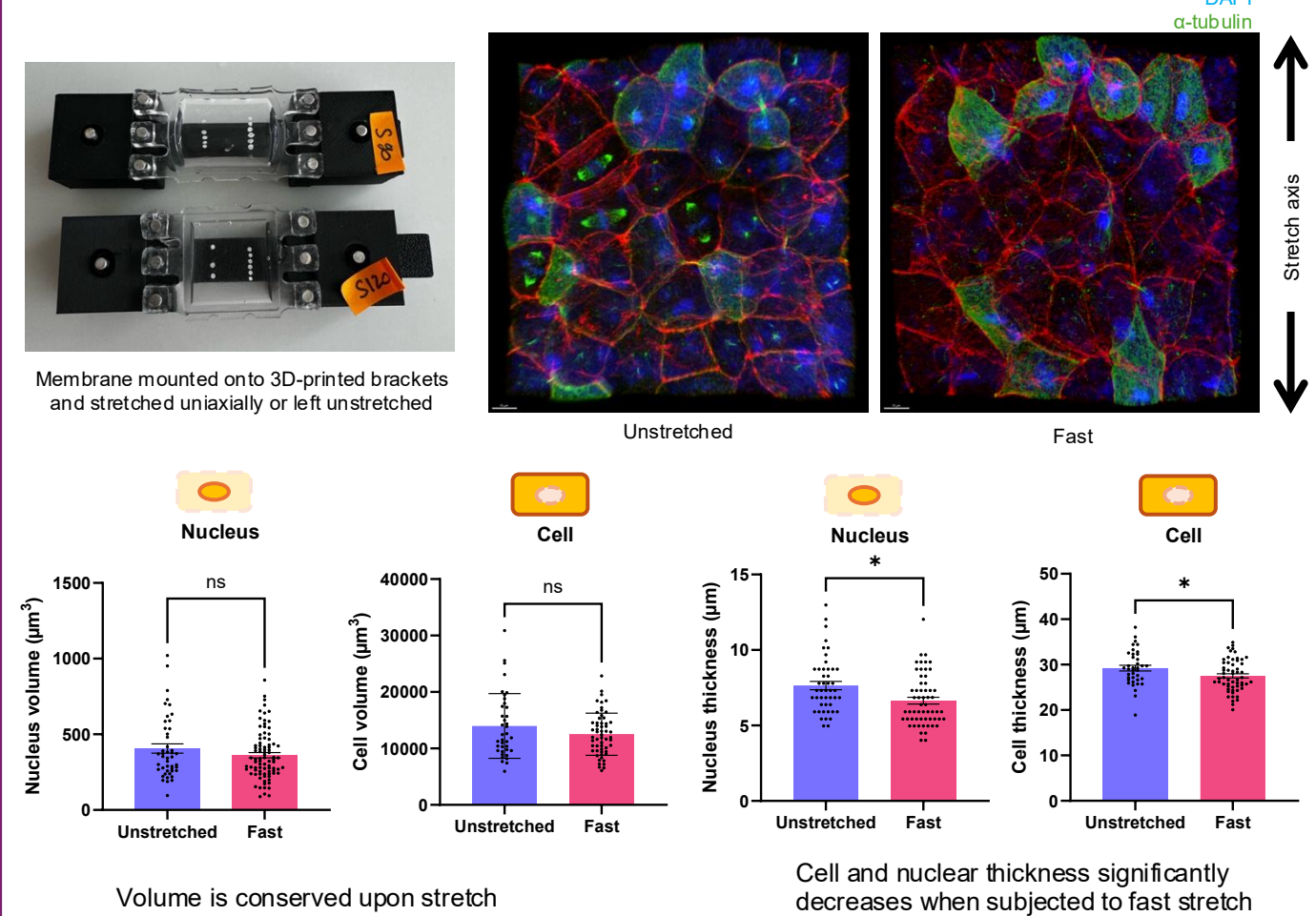
## Methods



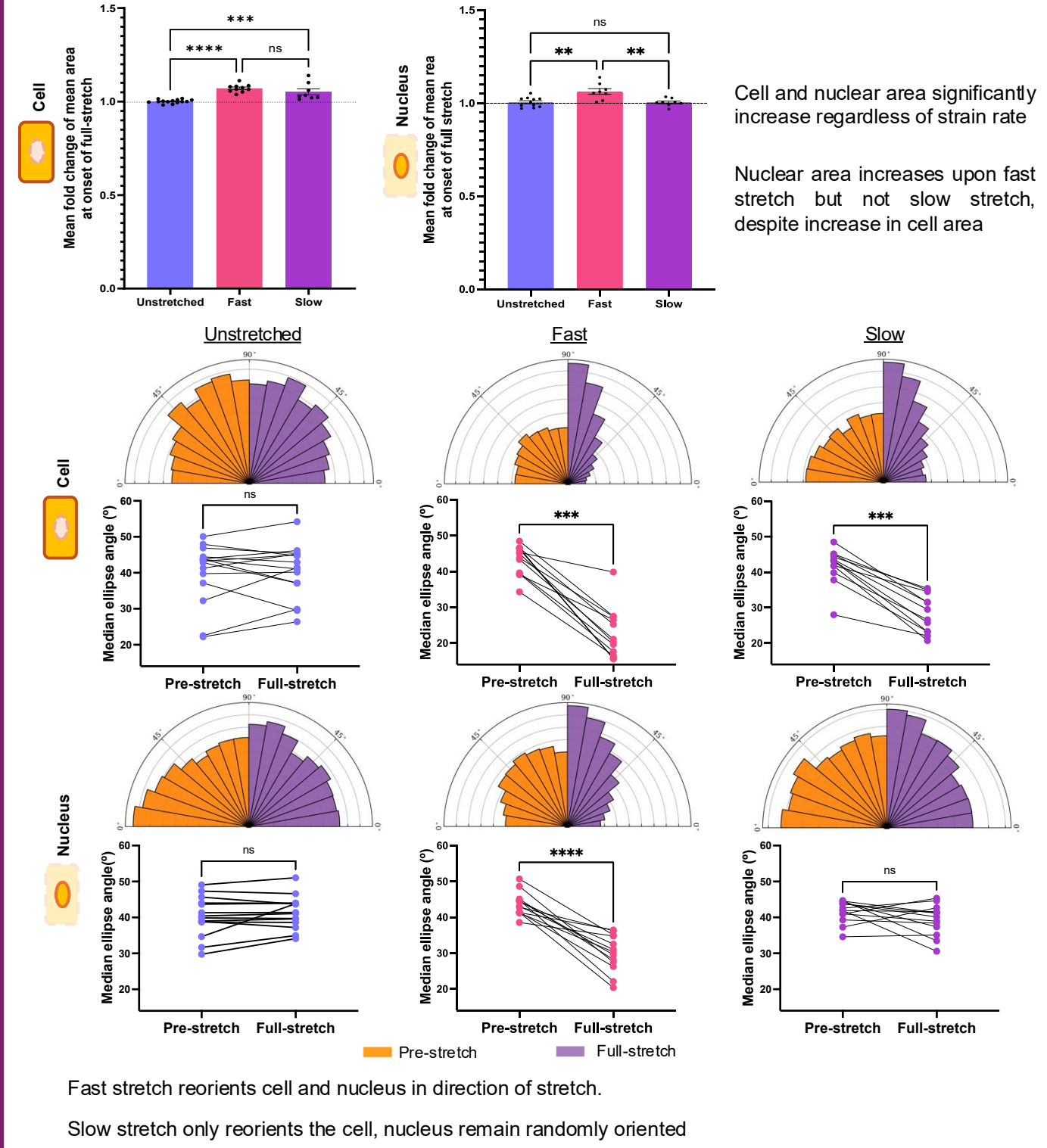
## 1. Fast stretch induces rapid mitotic entry



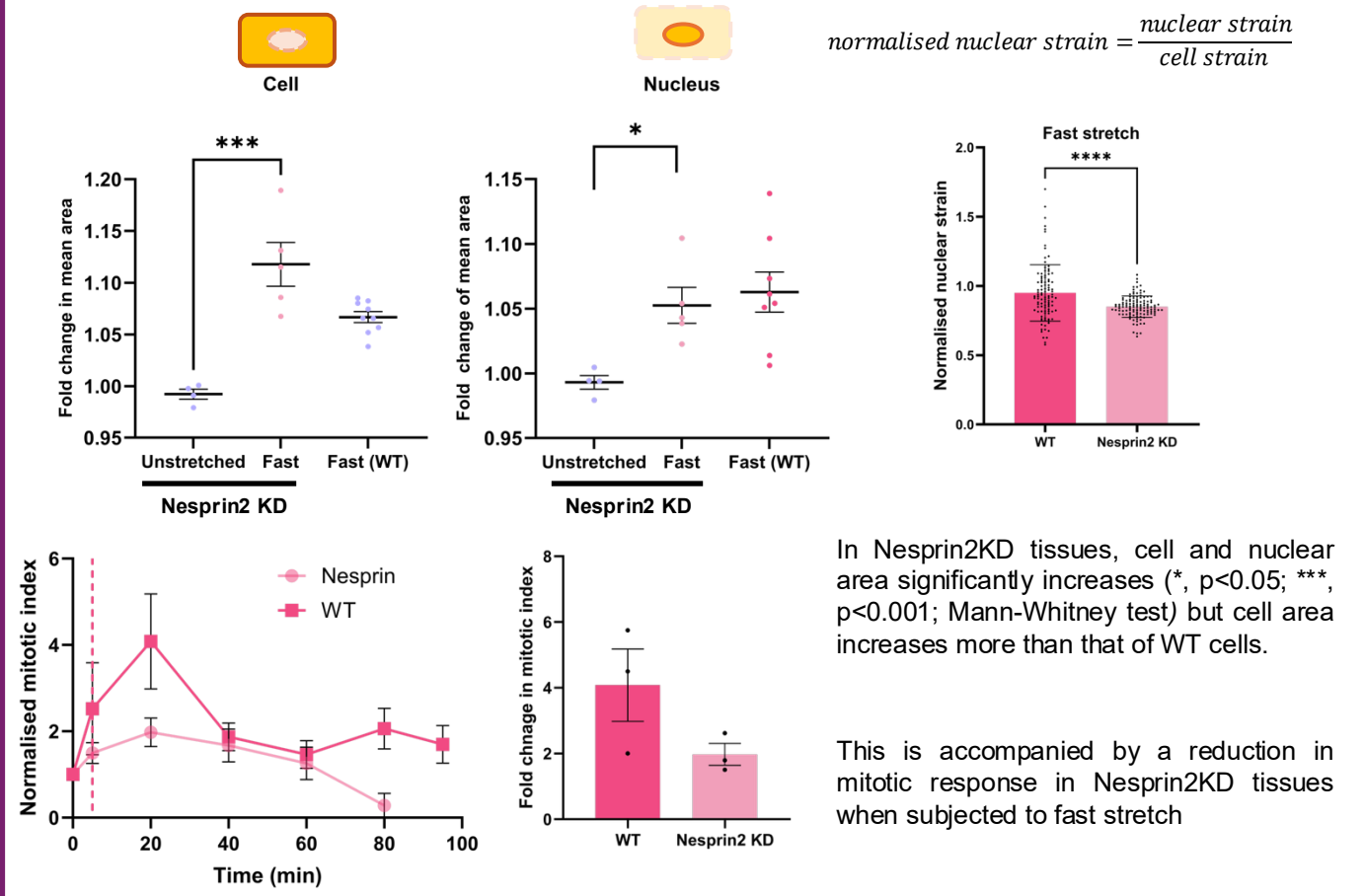
## 2. Fast stretch induces cell and nuclear flattening



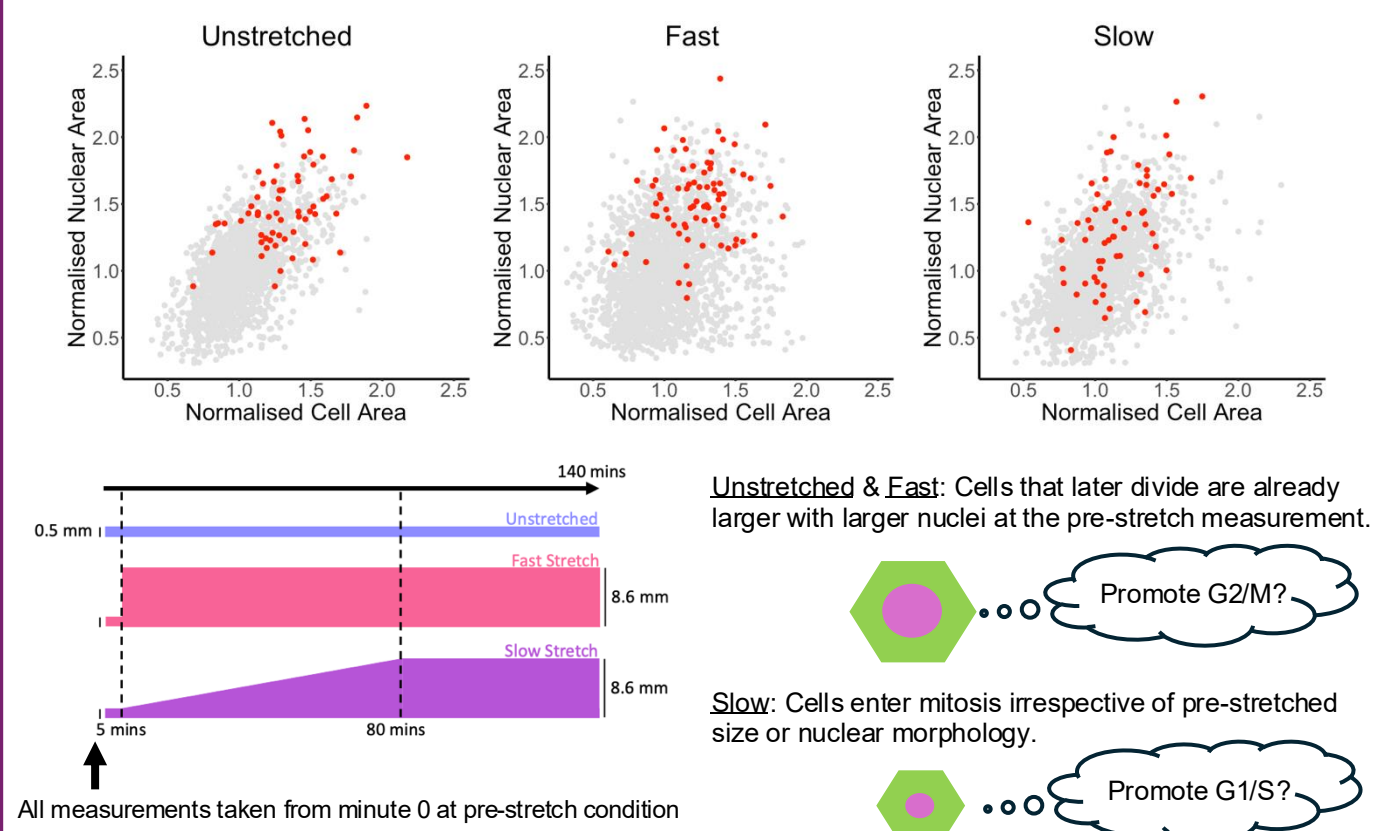
## 3. Slow stretch do not deform nuclei despite cell deformation



## 4. Nesprin2KD decouples cell and nuclear deformation and disrupts mitotic response



## 5. Slow stretch promotes mitosis on cells with specific morphology



## Conclusion

- Slow stretch does not upregulate mitotic entry, unlike fast stretch, and relative nuclear deformation could explain this difference in rates of mitotic entry.
- Nesprin2 is important in transmitting stretch to the nucleus and regulating cell division in response to mechanical stress.
- Fast stretch promotes rapid G2/M transition while slow stretch potentially push cells through S phase.

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