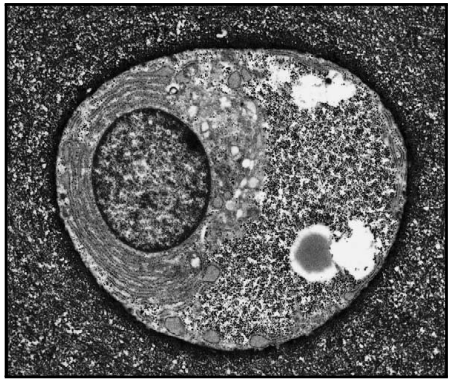
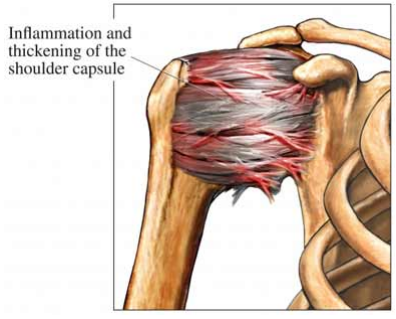
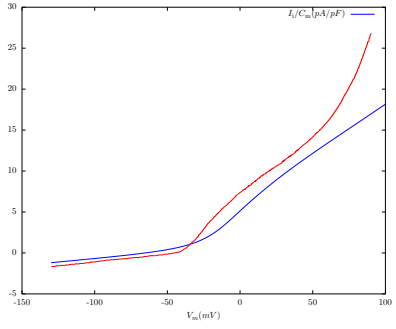
This talk will describe the status of our electrophysiological model of chondrocytes in human articular cartilage



What is the chondrocyte, and why is it interesting?

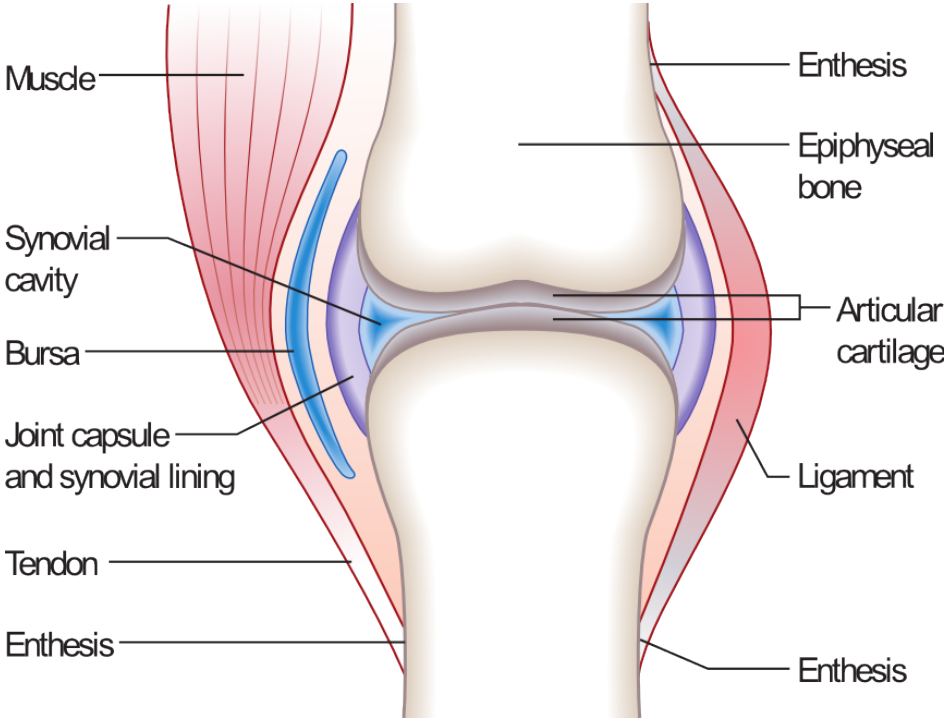


What are the specific questions we aim to answer?



How does our cellular model help us answer these questions?

Articular cartilage is the connective tissue that separates bones at joints, allowing them to slide past each other



Articular cartilage as part of a synovial joint

- Cartilage is composed of *chondrocytes*, an ECM (collagen and elastin) and proteoglycans
- The tissue is aneural, avascular and alymphatic and is thus slow to grow and heal

[Poole, 1997]

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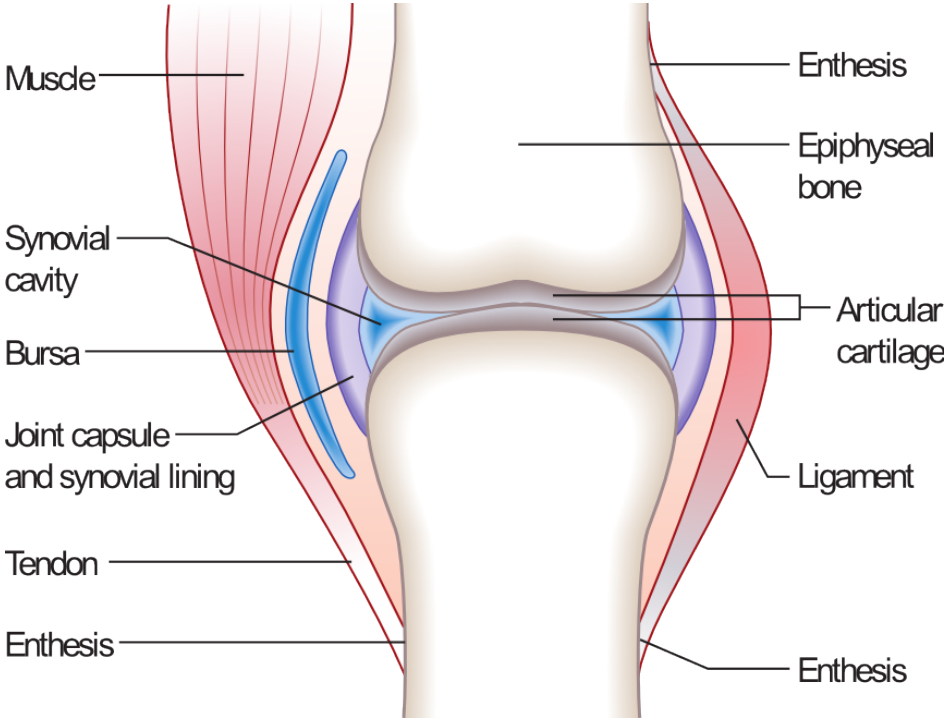

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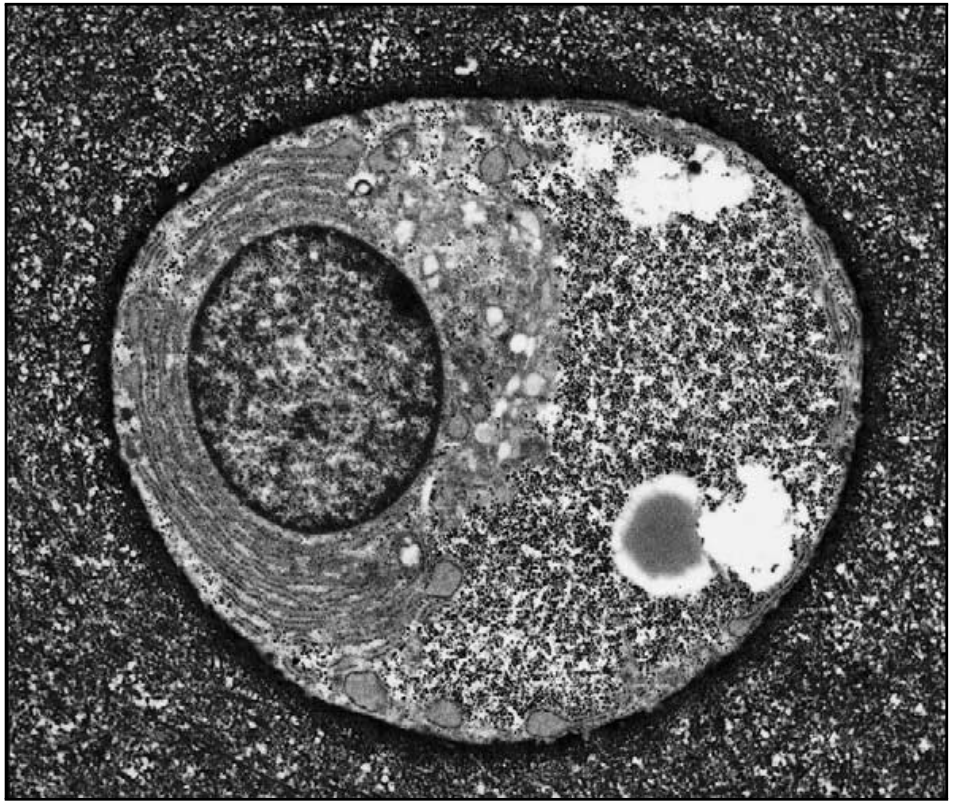
Chondrocytes are the resident cells of articular cartilage and are responsible for maintaining the extracellular matrix



Electron micrograph of typical chondrocyte

- Chondrocytes are isolated within a voluminous ECM
- Relies on diffusion from the articular surface for nutrient and metabolite exchange
- Sensitive to extra-cellular pH, ionic environment, stress state
- Arthritis is the associated degenerative pathology

[Archer & Francis-West 2003]

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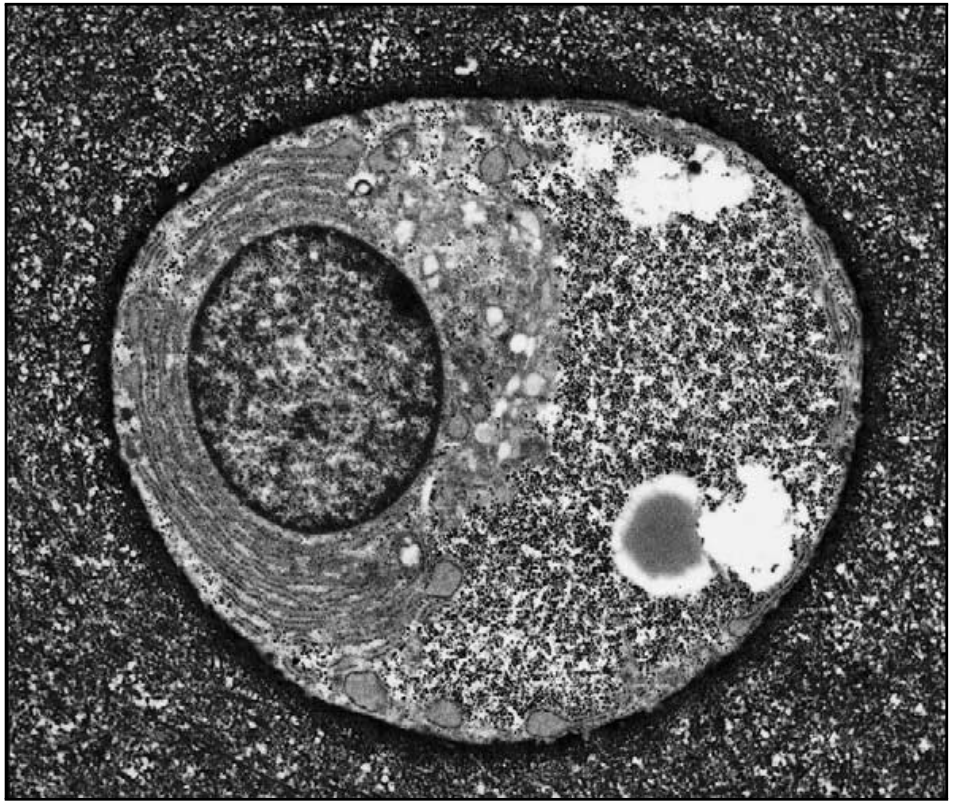

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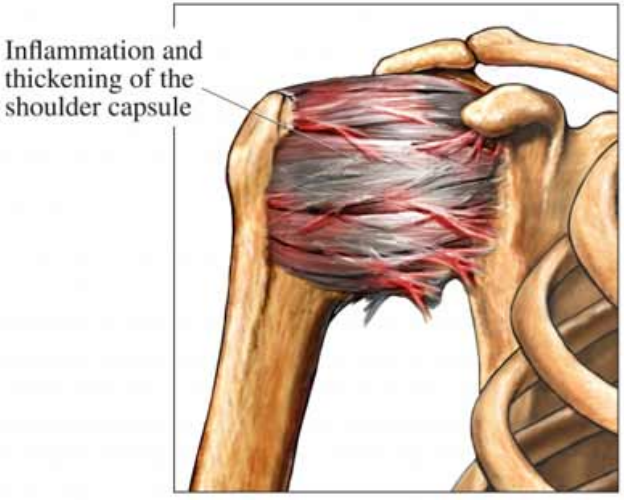
We narrow our focus to a specific question to motivate our initial modelling effort



What causes the "frozen shoulder syndrome" when tissue is exposed to the local anæsthetic bupivacaine?

- How does the cell survive in an acidic environment and still continue to synthesise and maintain viable cartilage?
- How does the chondrocyte "sense" and respond to loading?

[Webb, 2009; Hall et al., 1996]

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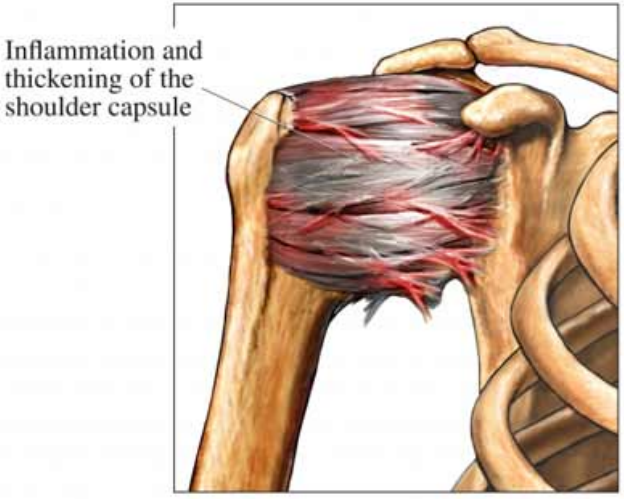

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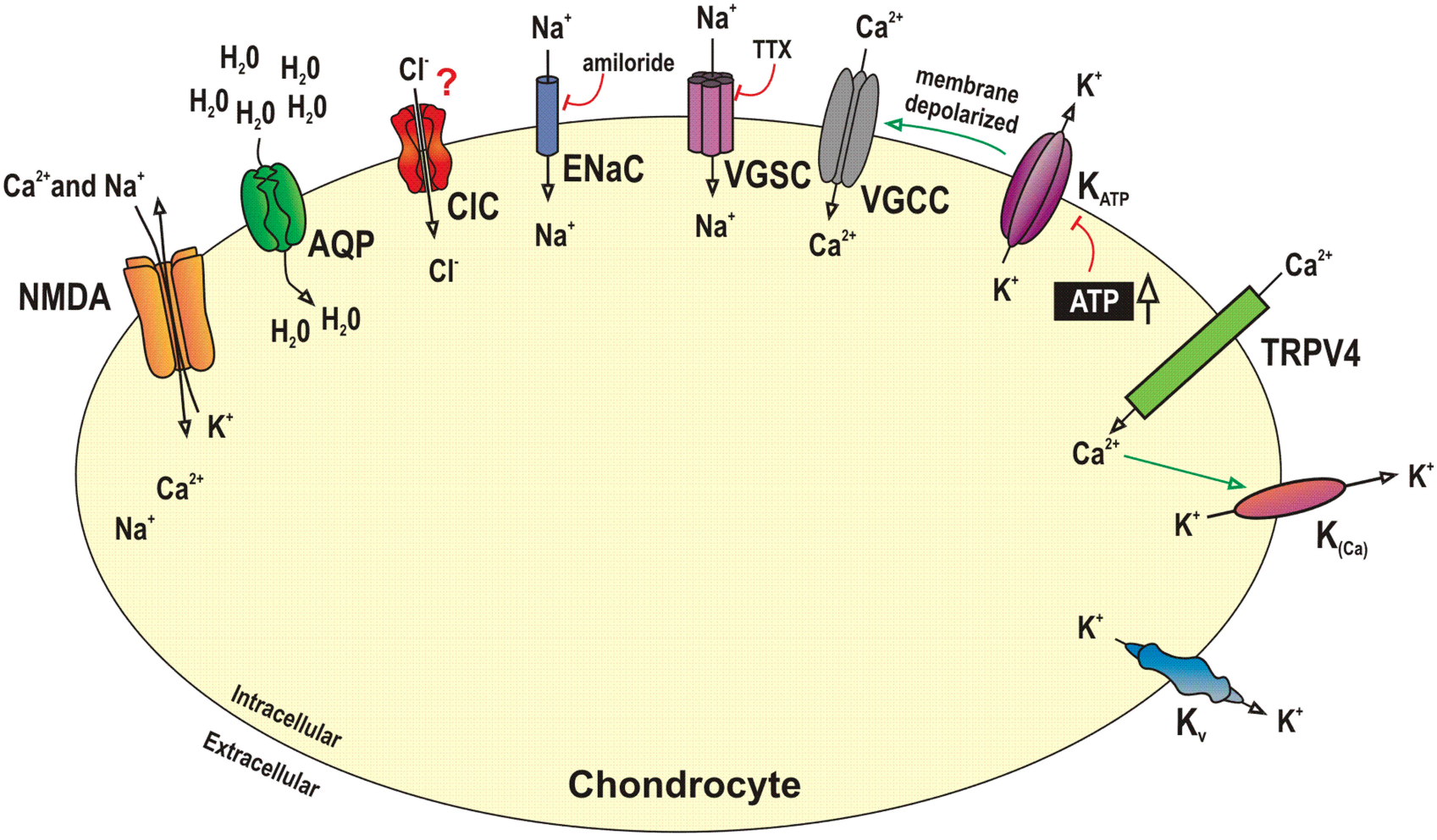
[Webb, 2009; Hall et al., 1996]

In order to answer such questions, we need a model that helps us understand some fundamental things

- The important important ion channels of the cell
- The basis of the resting membrane potential
- The role of cellular volume regulation

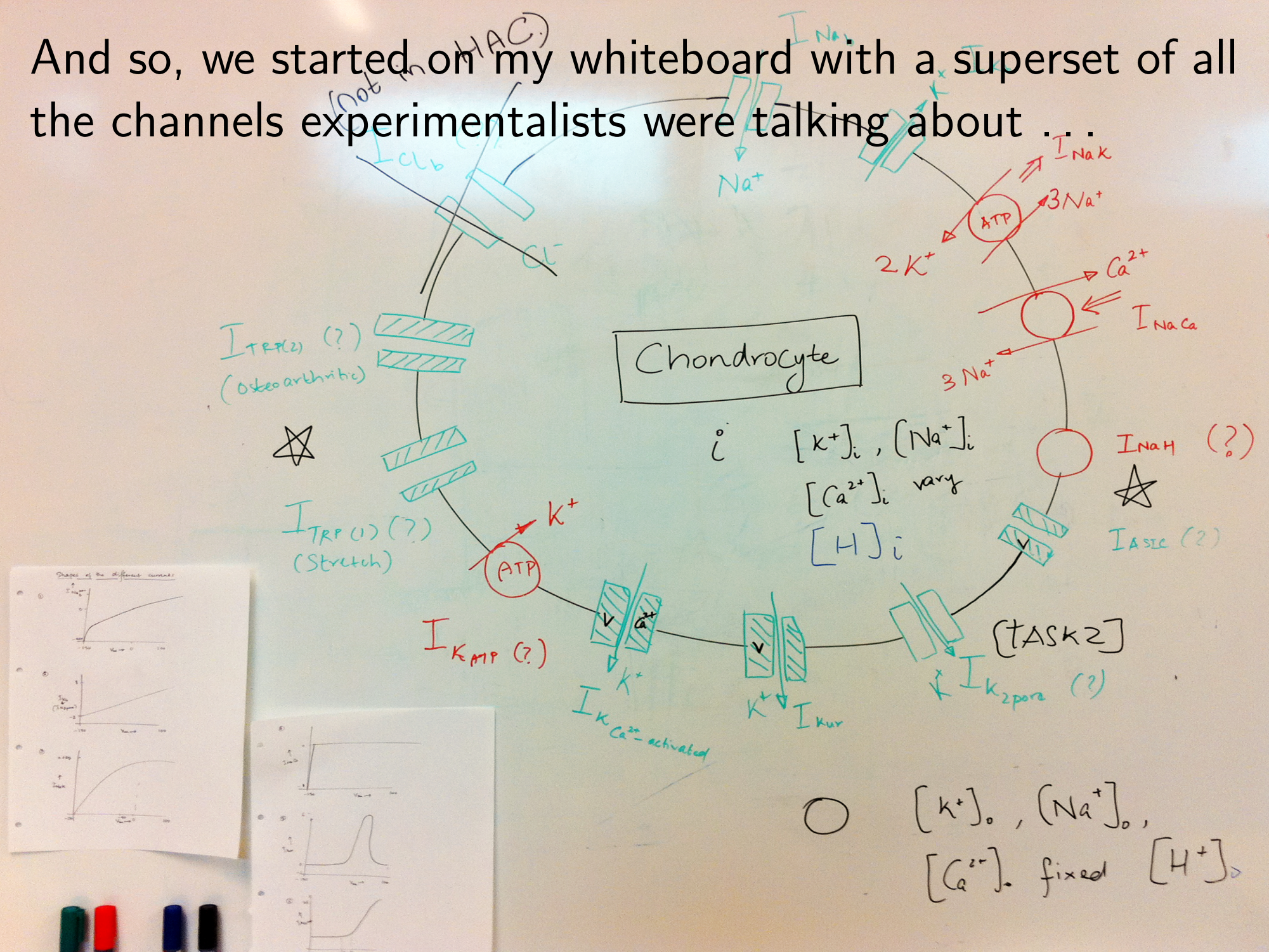
[Lewis et al., 2011]

Physiology literature gives us a broad overview of the ion channels present in chondrocytes

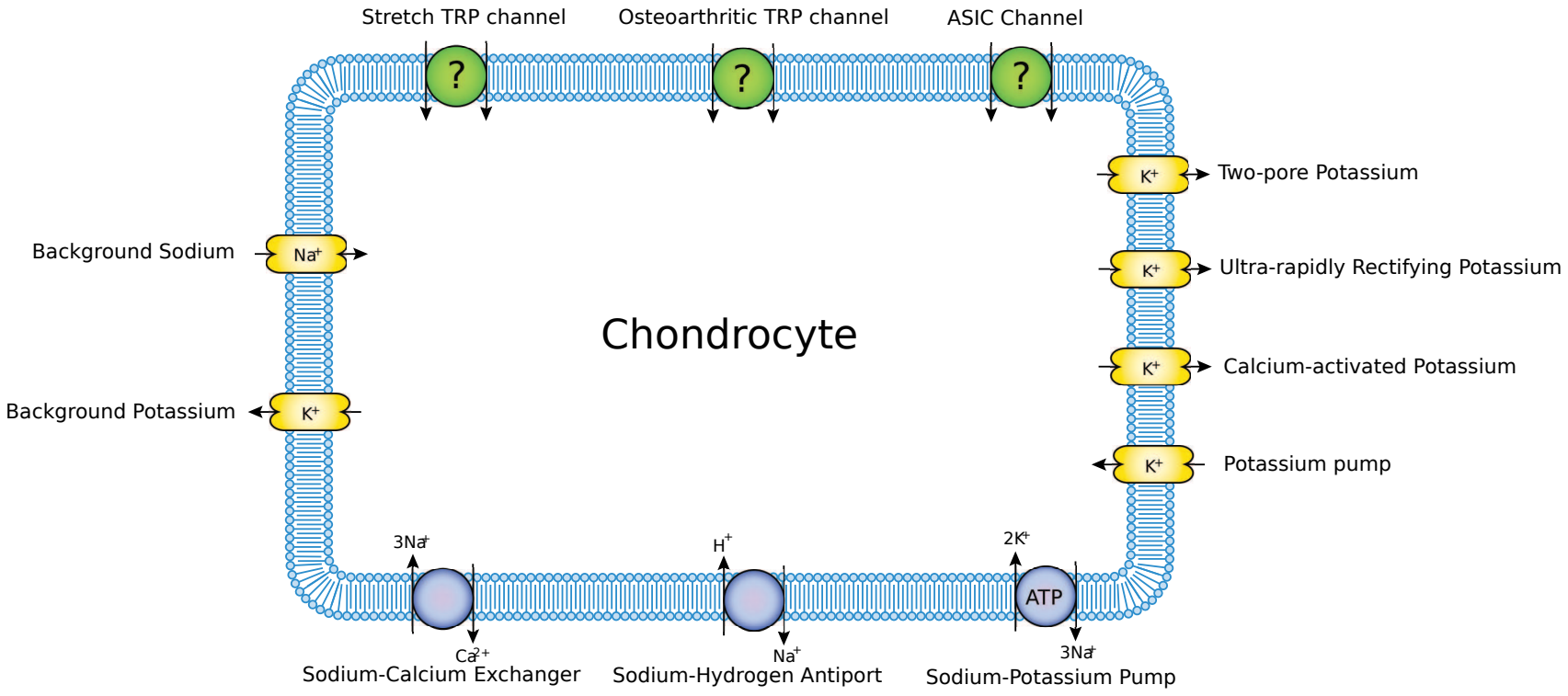


[Hall et al., 1996; Barrett-Jolley et al., 2010]

And so, we started on my whiteboard with a superset of all the channels experimentalists were talking about . . .



. . . simplified things a little, and arrived at our electrophysiological model of a single chondrocyte



Our ion channel model of a single chondrocyte

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$$
\begin{aligned}
-C_{\mathrm{m}}\frac{dV_{\mathrm{m}}}{dt} = & \underbrace{I_{\mathrm{Na_b}} + I_{\mathrm{K_b}}}_{\text{Background currents}} \\
& + \underbrace{I_{\mathrm{NaK}} + I_{\mathrm{NaCa}} + I_{\mathrm{NaK}}}_{\text{Pumps and exchangers}} \\
& + \underbrace{I_{\mathrm{K_{ur}}} + I_{\mathrm{K_{2\,pore}}} + I_{\mathrm{K_{Ca-act}}} + I_{\mathrm{K_{ATP}}}}_{\text{Potassium channels}} \\
& + \underbrace{I_{\mathrm{ASIC}} + I_{\mathrm{TRP1}} + I_{\mathrm{TRP2}} + I_{\mathrm{stim}}}_{\text{Other currents}}
\end{aligned}
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For more details on the model and how it is implemented, let us step into the code for a quick demo

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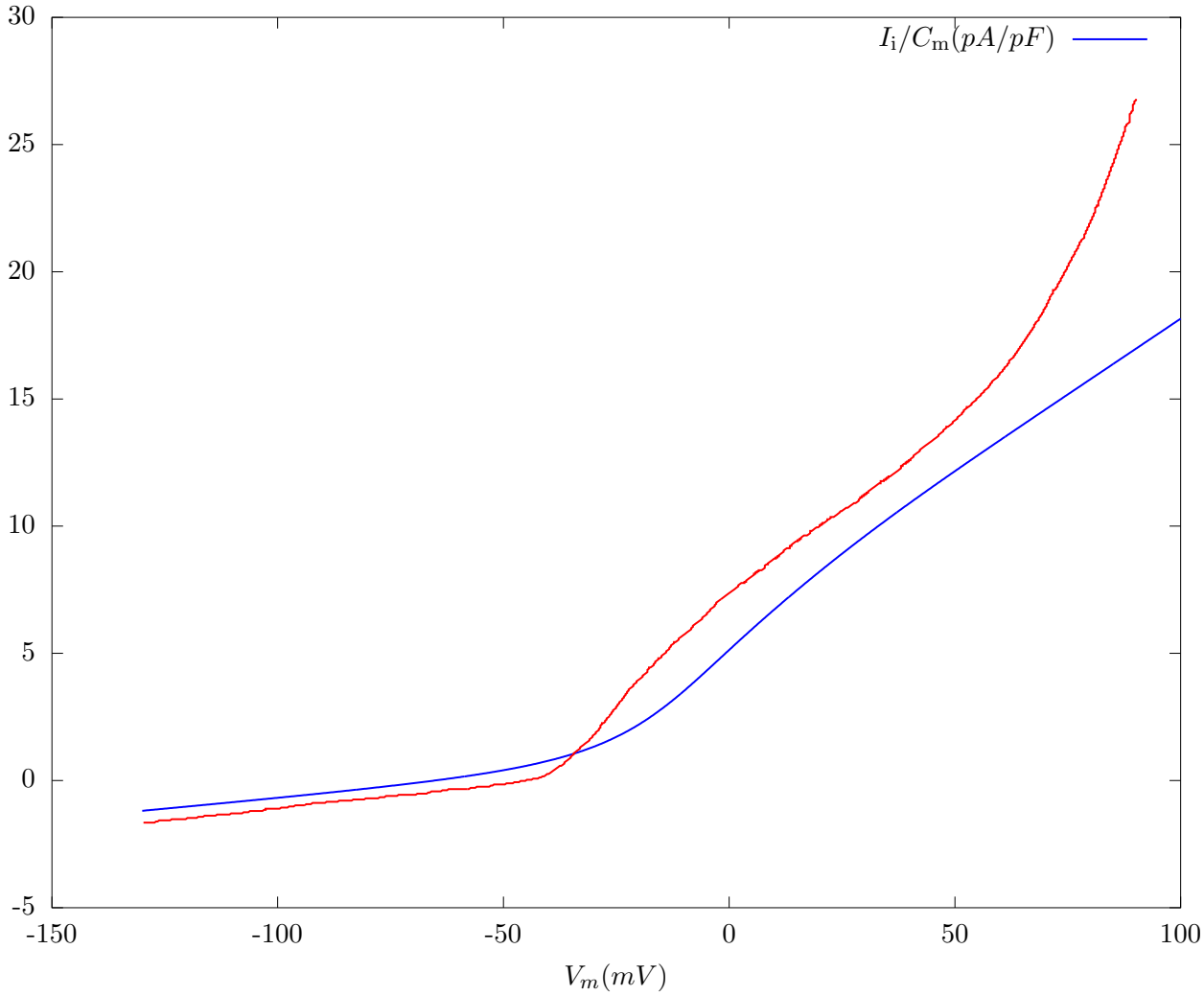
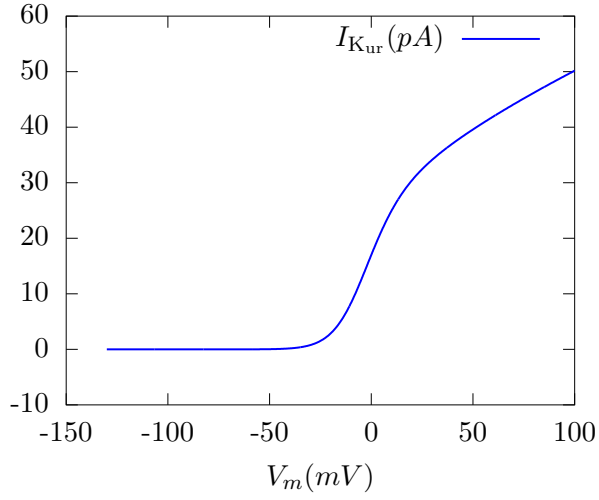
[Hindmarsh, 2001]

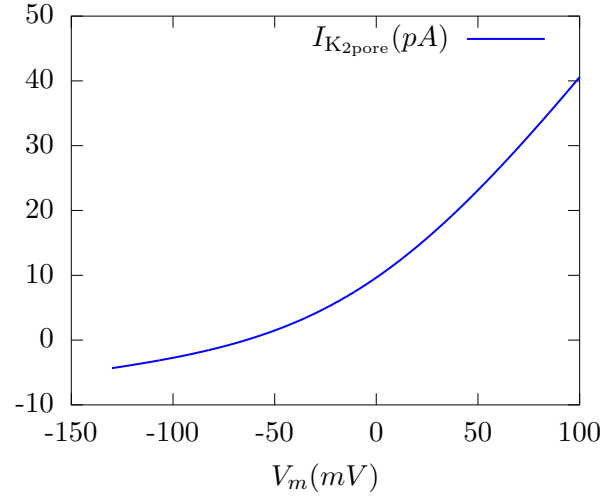
At the moment, I am completing the implementation and starting to tune parameters

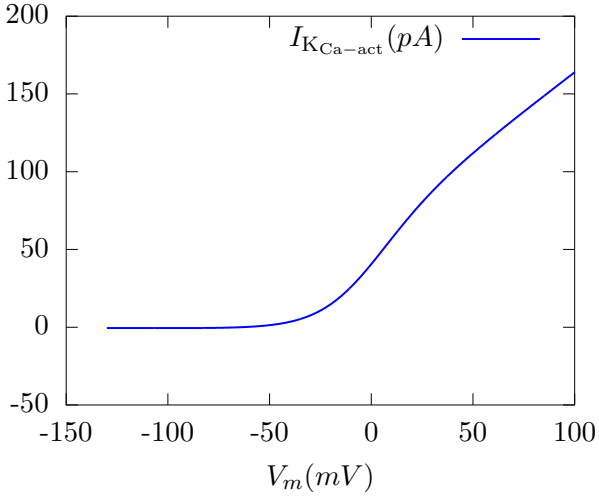


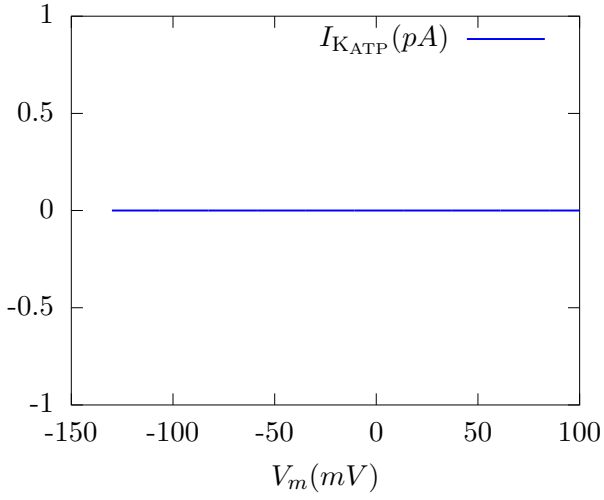
[Clark et. al., 2011; Millward-Sadler et. al., 2000]

Potassium channels seem to have a role in the frozen shoulder syndrome









So over the course of this talk, we . . .

- Learnt a bit about the physiology of the chondrocyte
- Got introduced to some interesting questions
- Arrived at a basic model to answer these questions

And in the future, we will:

- Continue to tune and benchmark the model
- Take a closer look at the implications of the calculations
- Expand to tissue level models to study stress response

[`https://bitbucket.org/harish/chondrocyte-model/`]

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