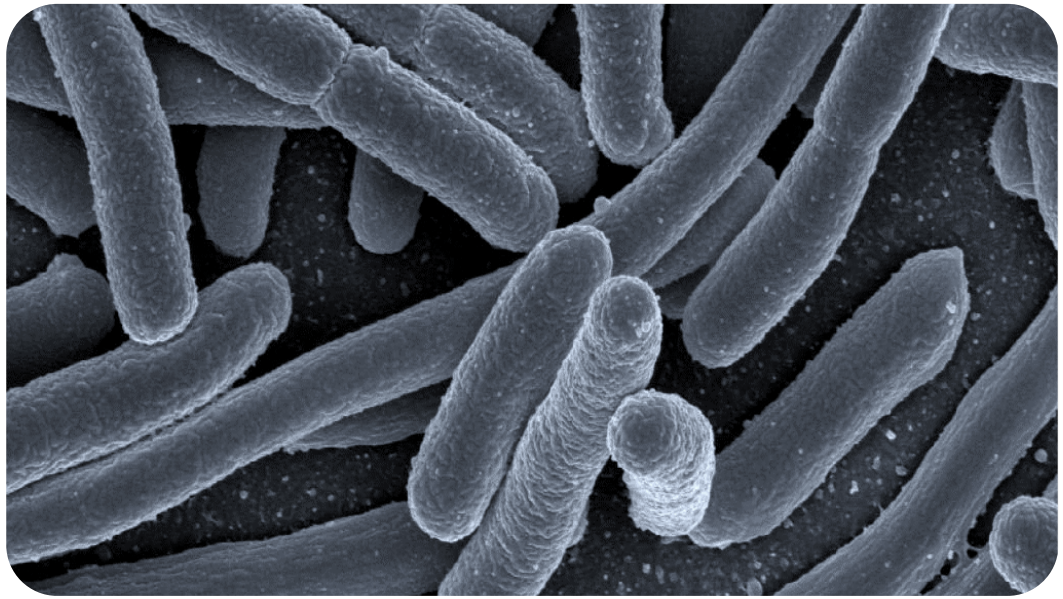
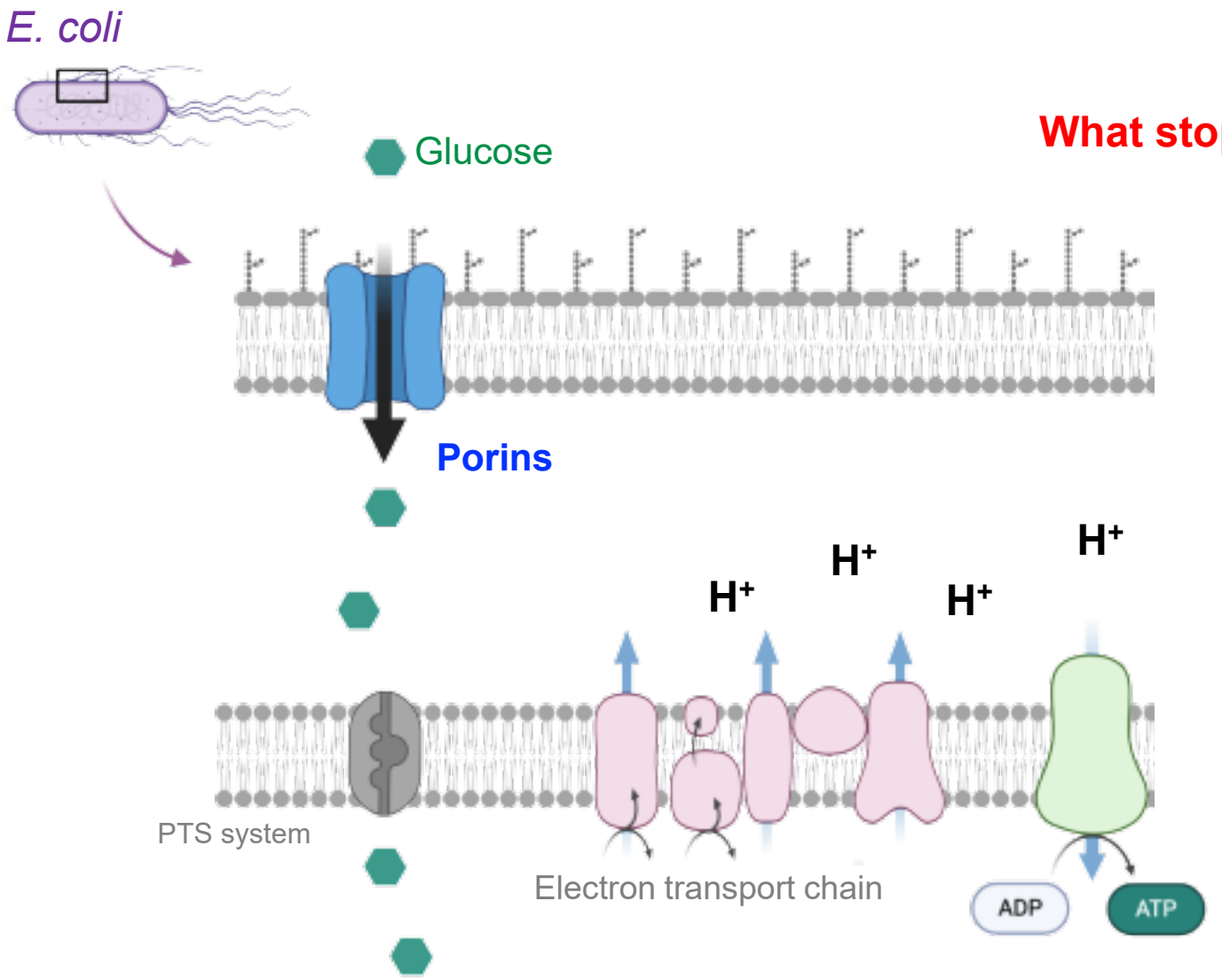
Periplasmic ions control bacterial permeability



Santiago Caño-Muñiz

PhD student
Floto Group
University Molecular Immunity Unit

How do bacteria balance eating with respiration?



What stops proton loss through porins?

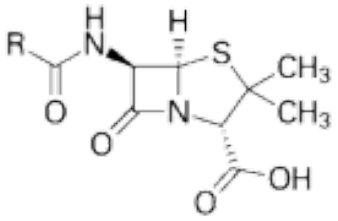
Outside

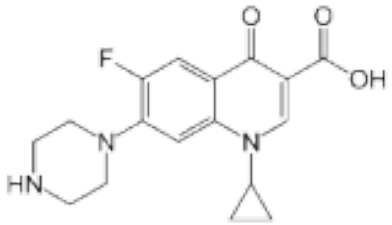
Periplasm

Cytoplasm

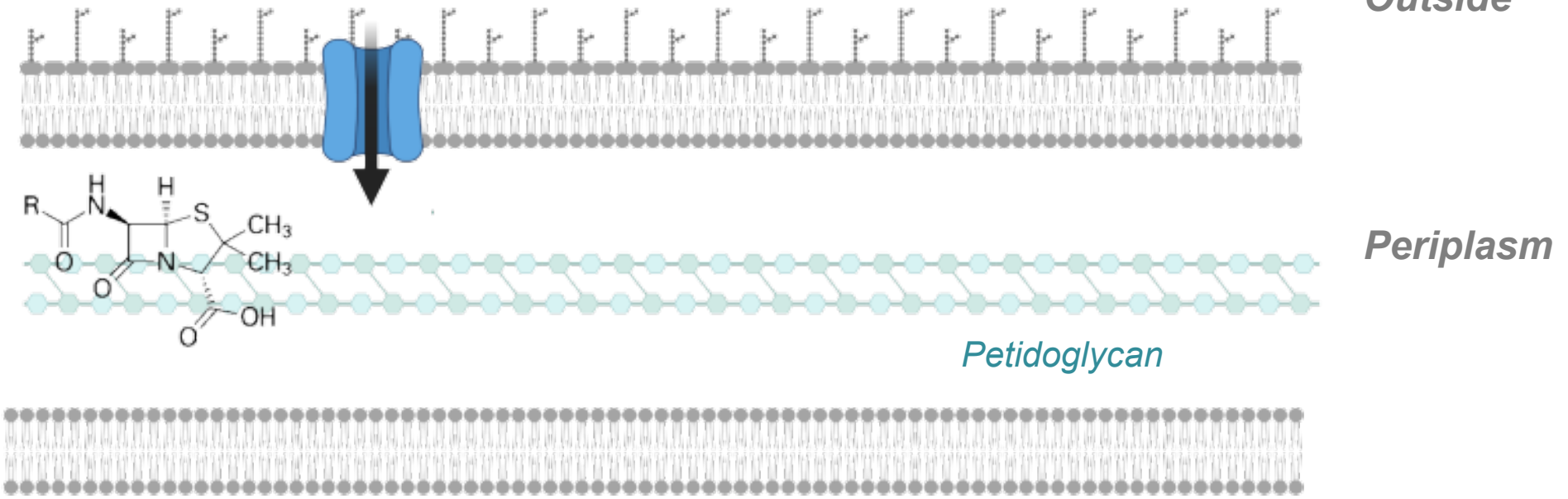
Porin permeability also influences antibiotic susceptibility

Penicillins





Ciprofloxacin

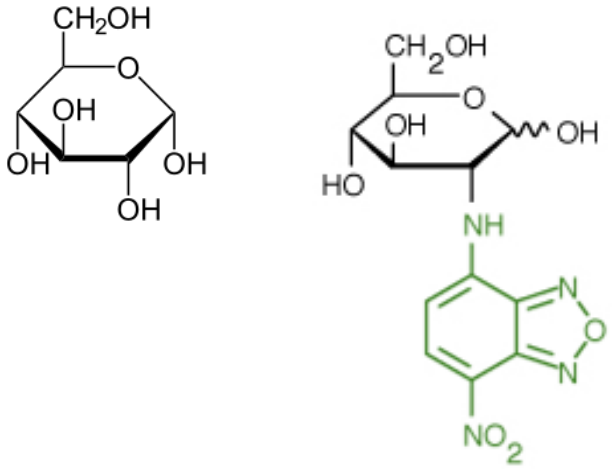


Do bacteria actively regulate porin permeability?

And, if so, how is this achieved?

Measuring porin permeability using a fluorescent glucose analogue

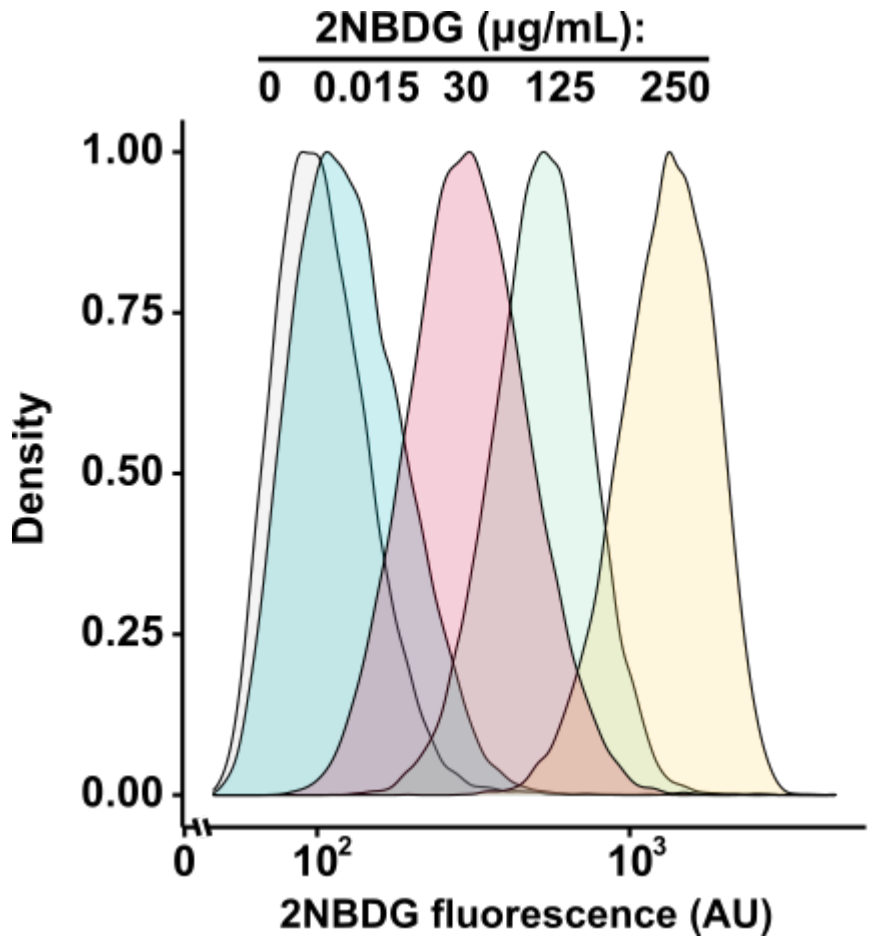
Glucose **2-NBDG**



Quantify bacterial uptake by Flow cytometry (FACS)

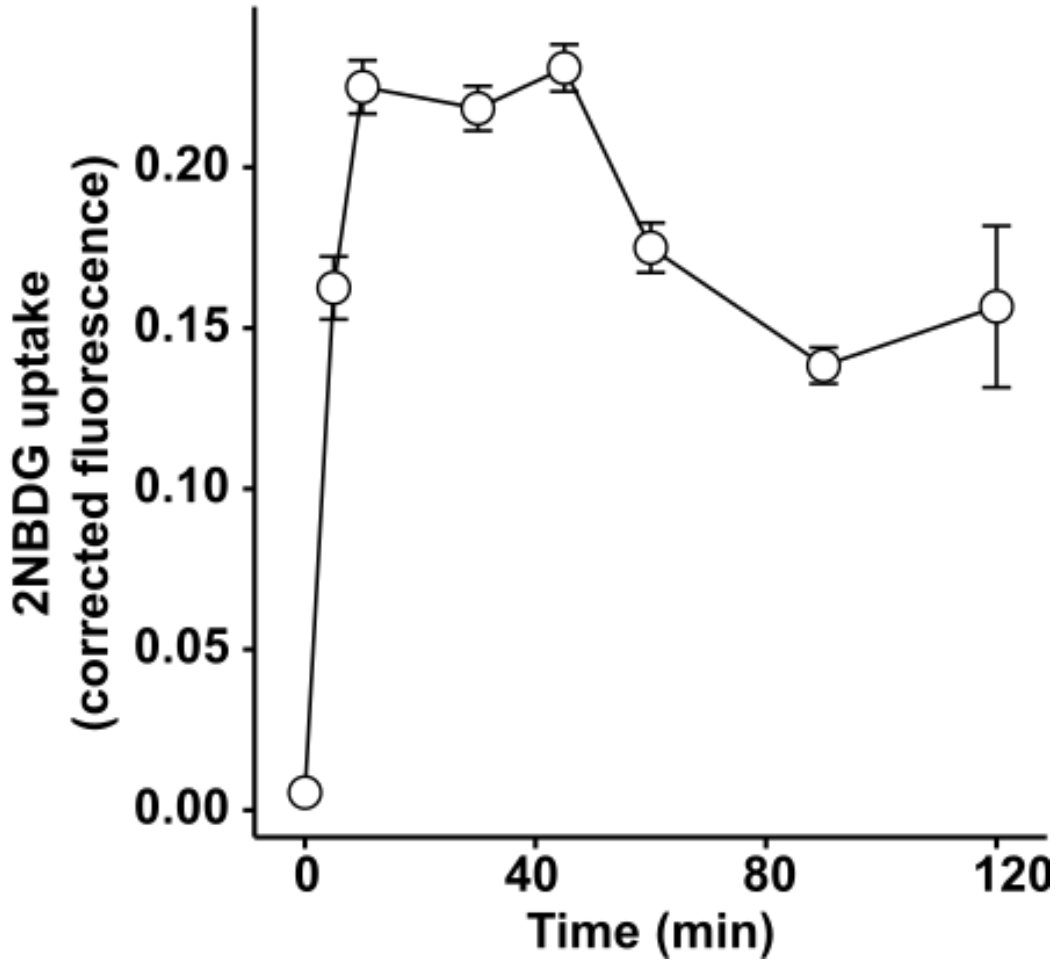
Measuring porin permeability using a fluorescent glucose analogue

Over different concentrations

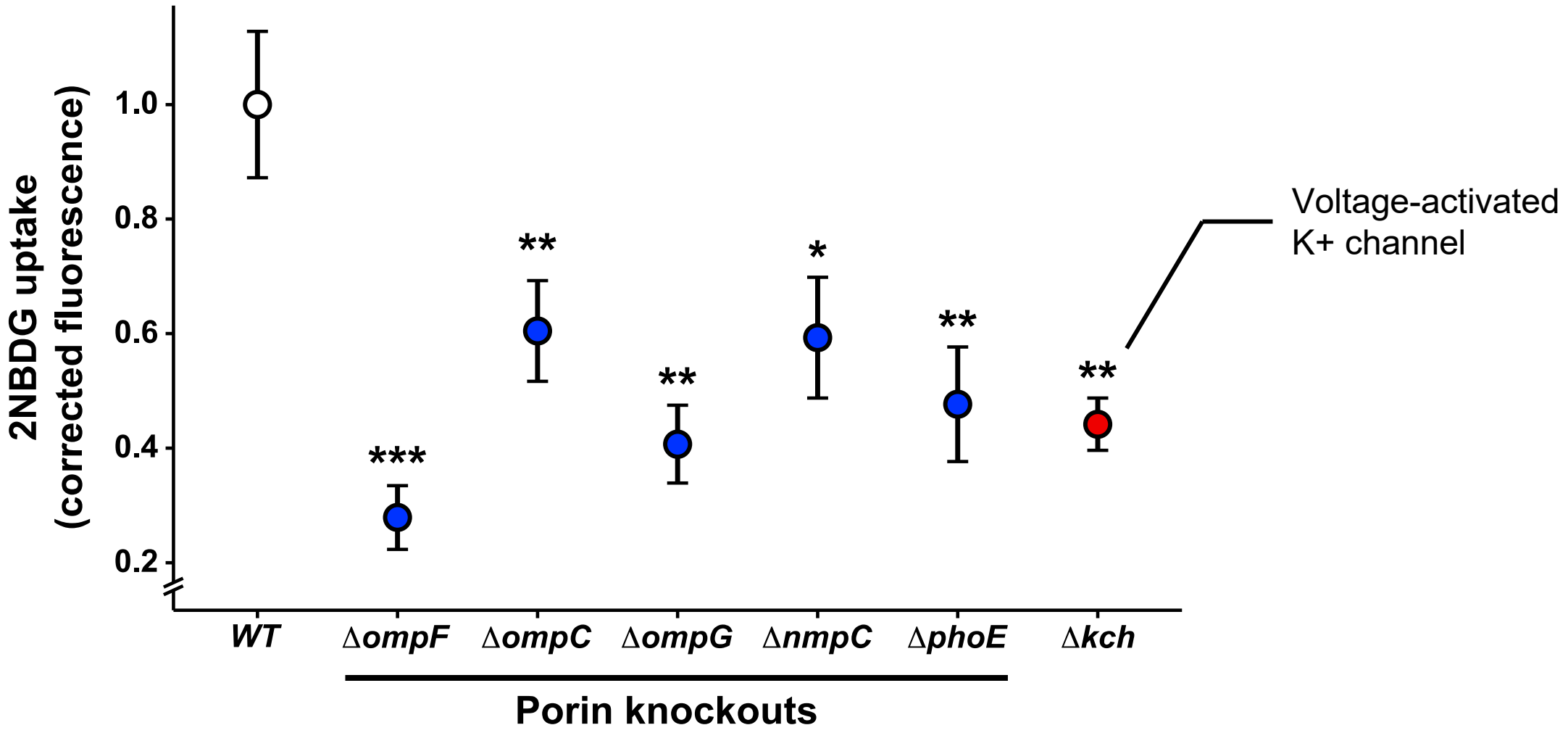


Measuring porin permeability using a fluorescent glucose analogue

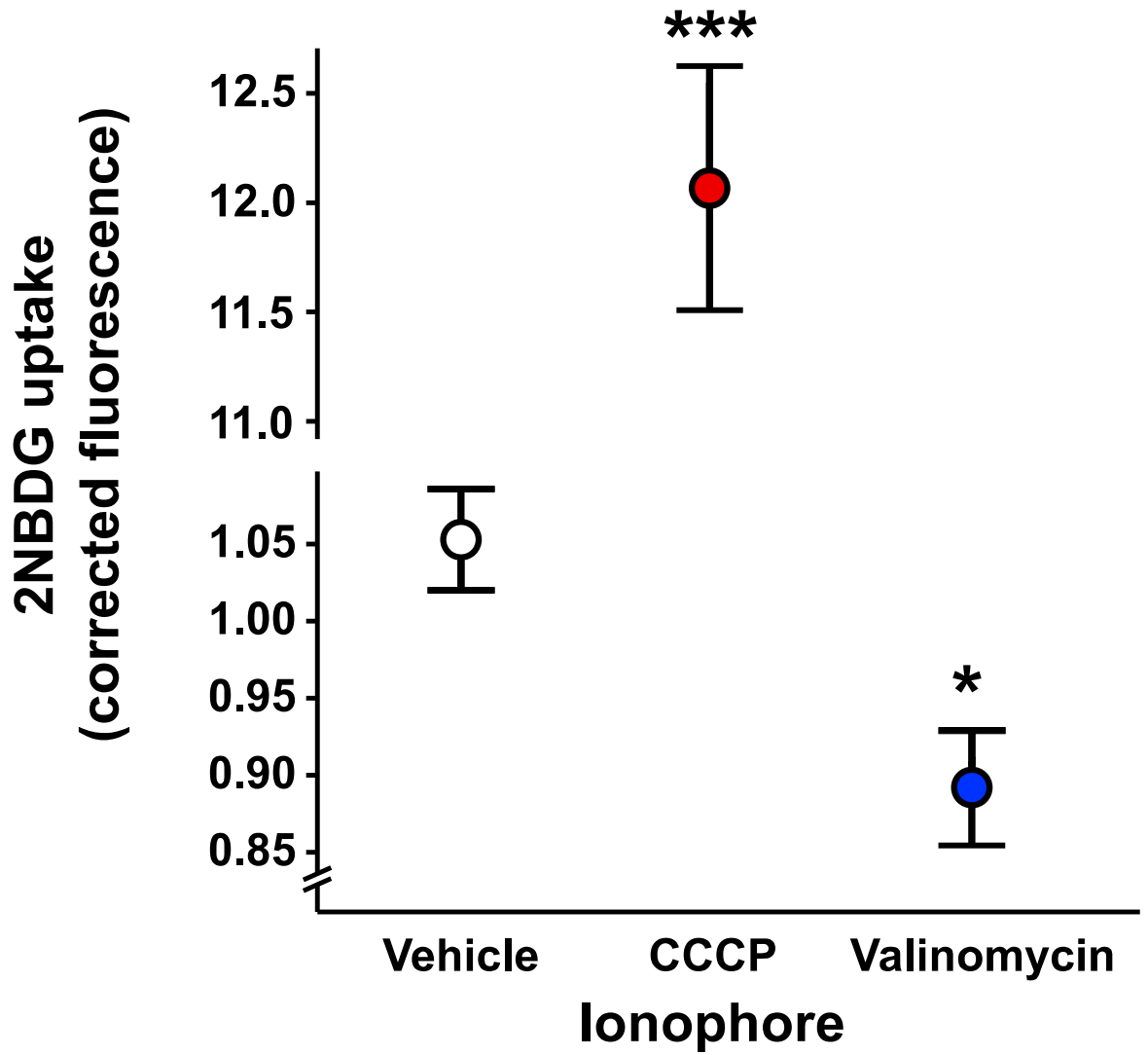
Over time



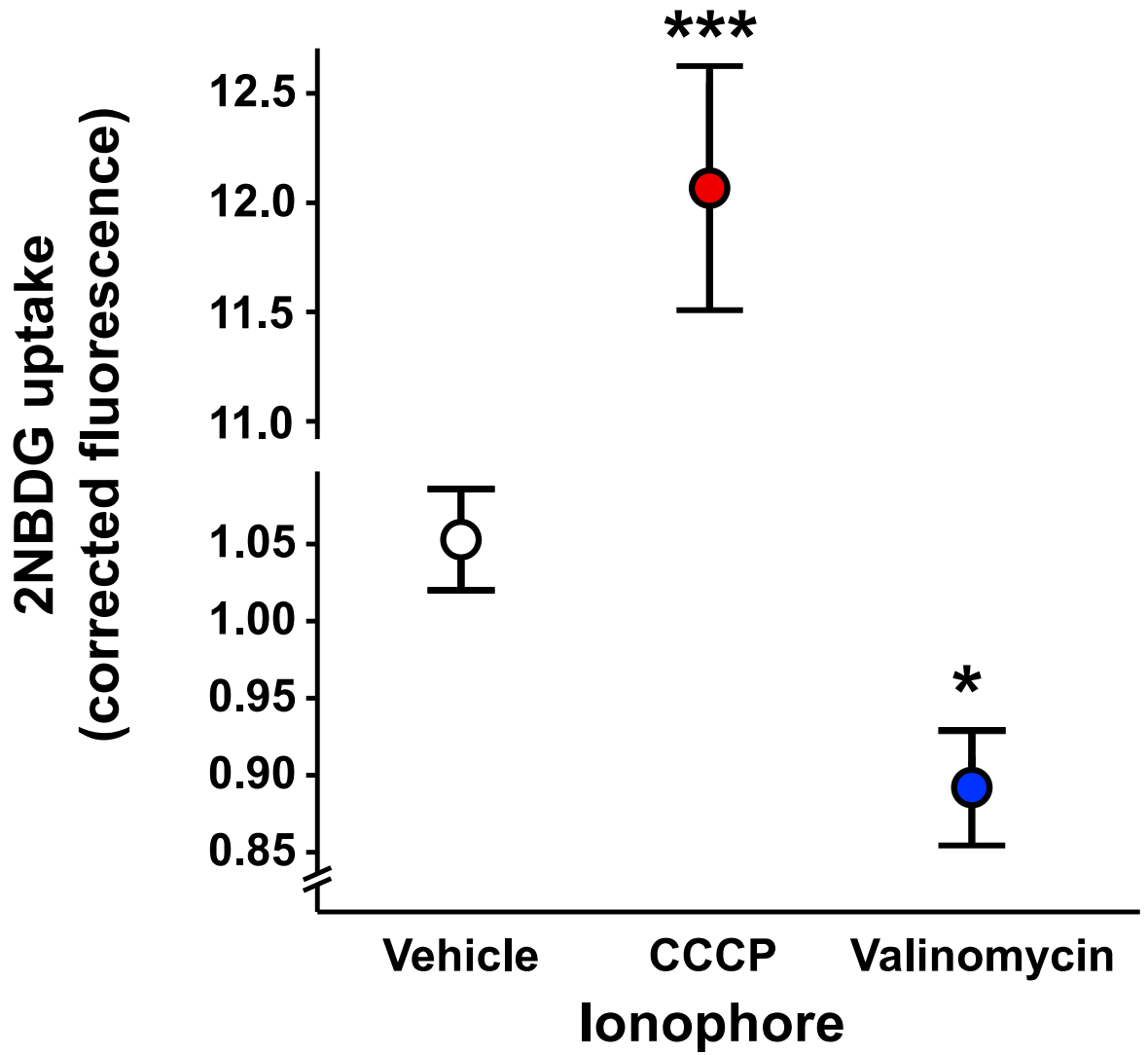
Porin permeability is regulated by ion channels



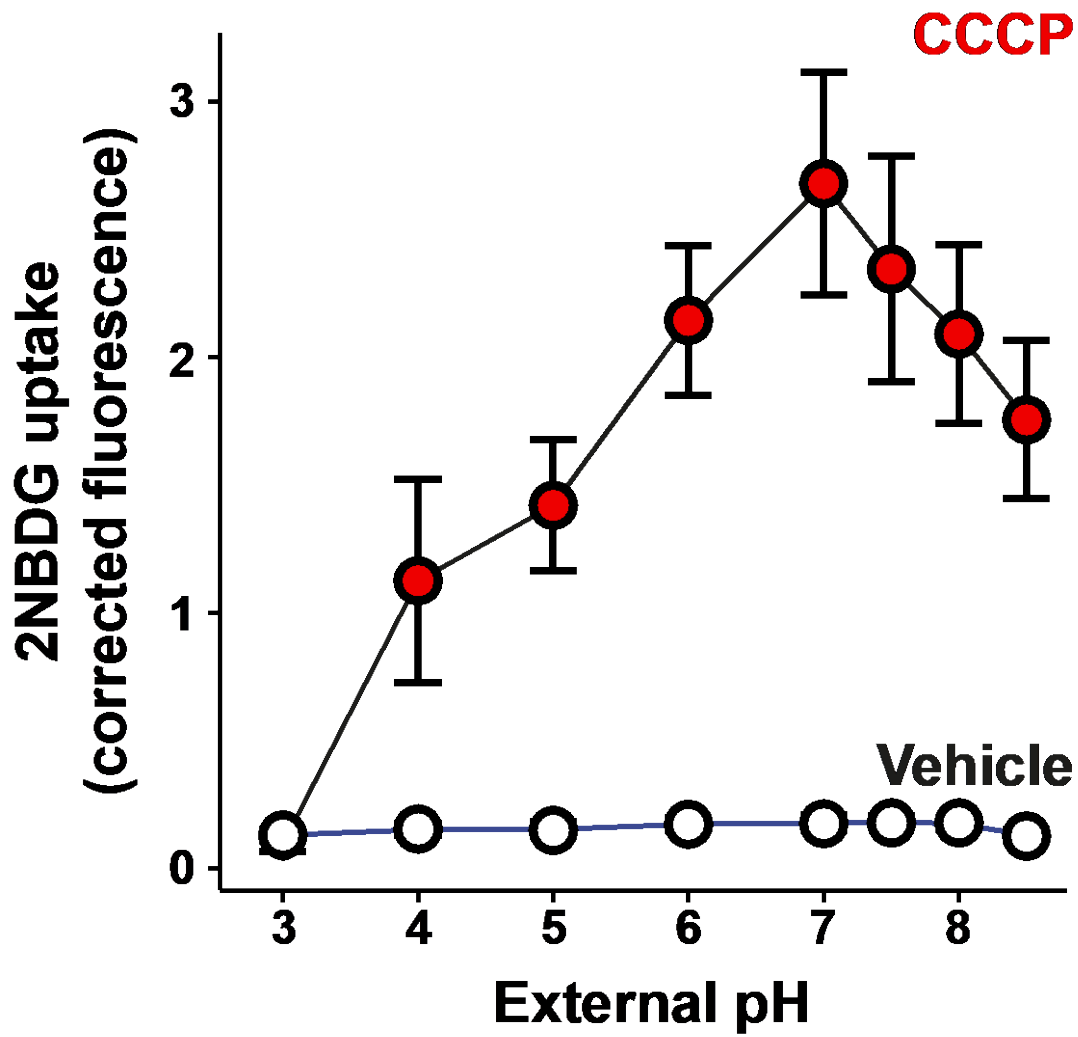
Porin permeability is regulated by H+ and K+ ions



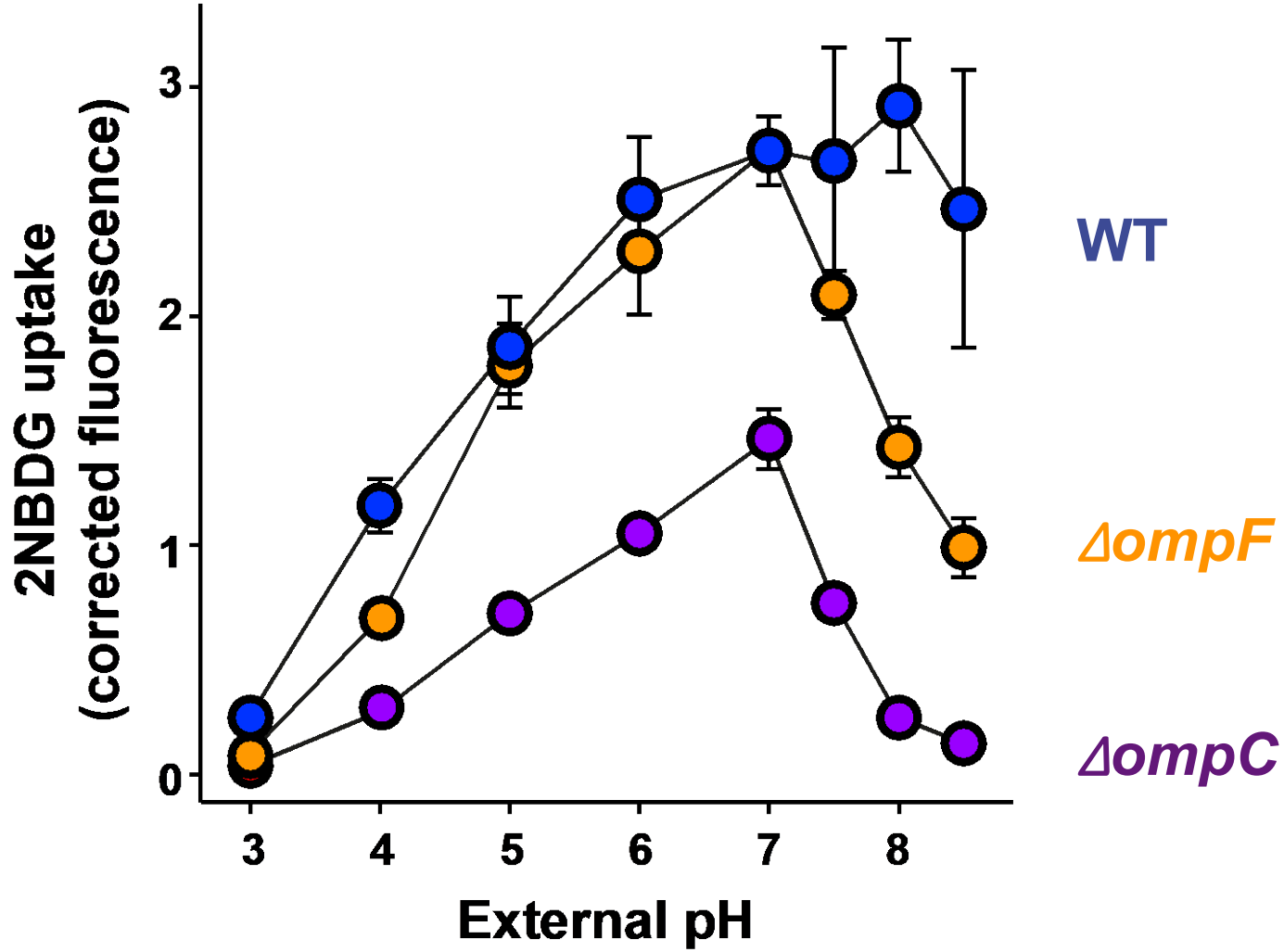
Porin permeability is regulated by H+ and K+ ions



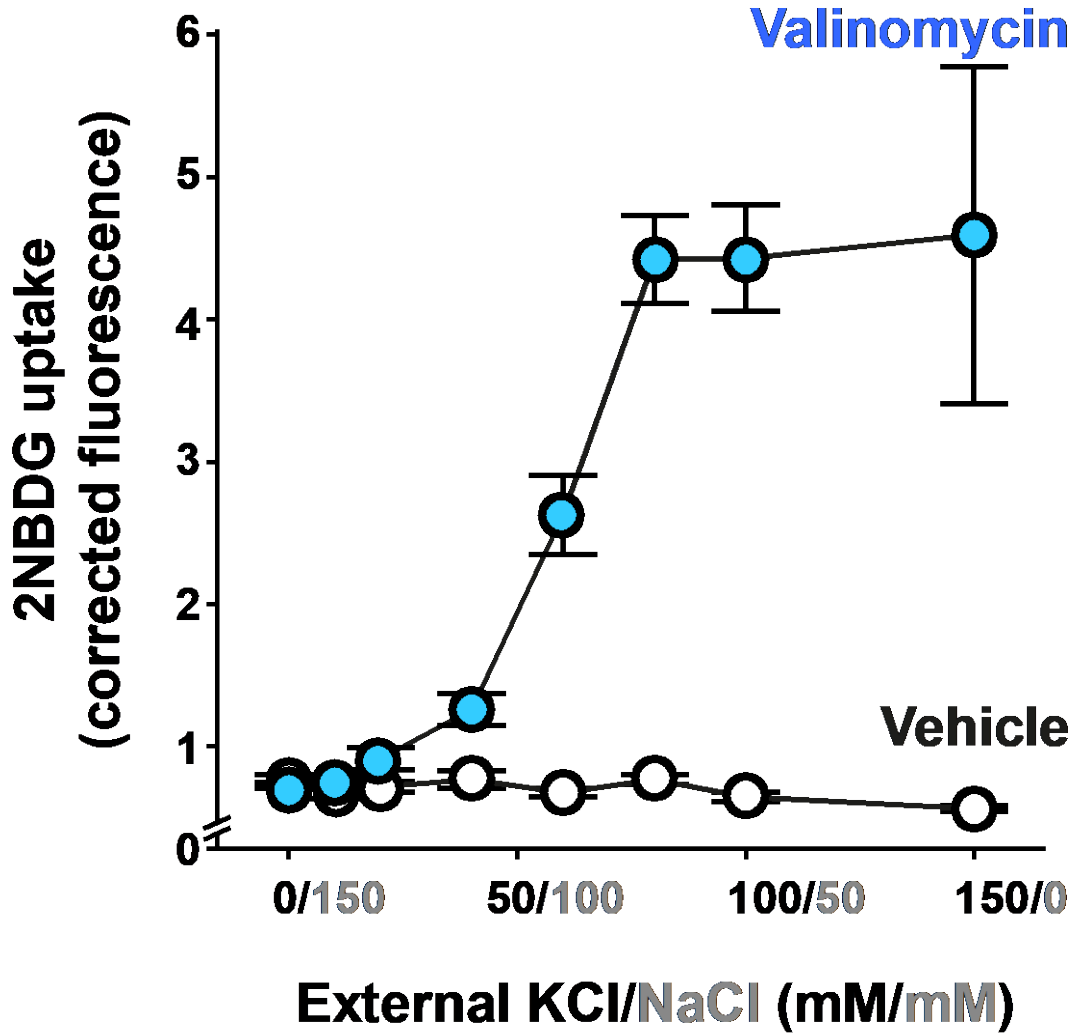
Porin permeability is regulated by internal H+



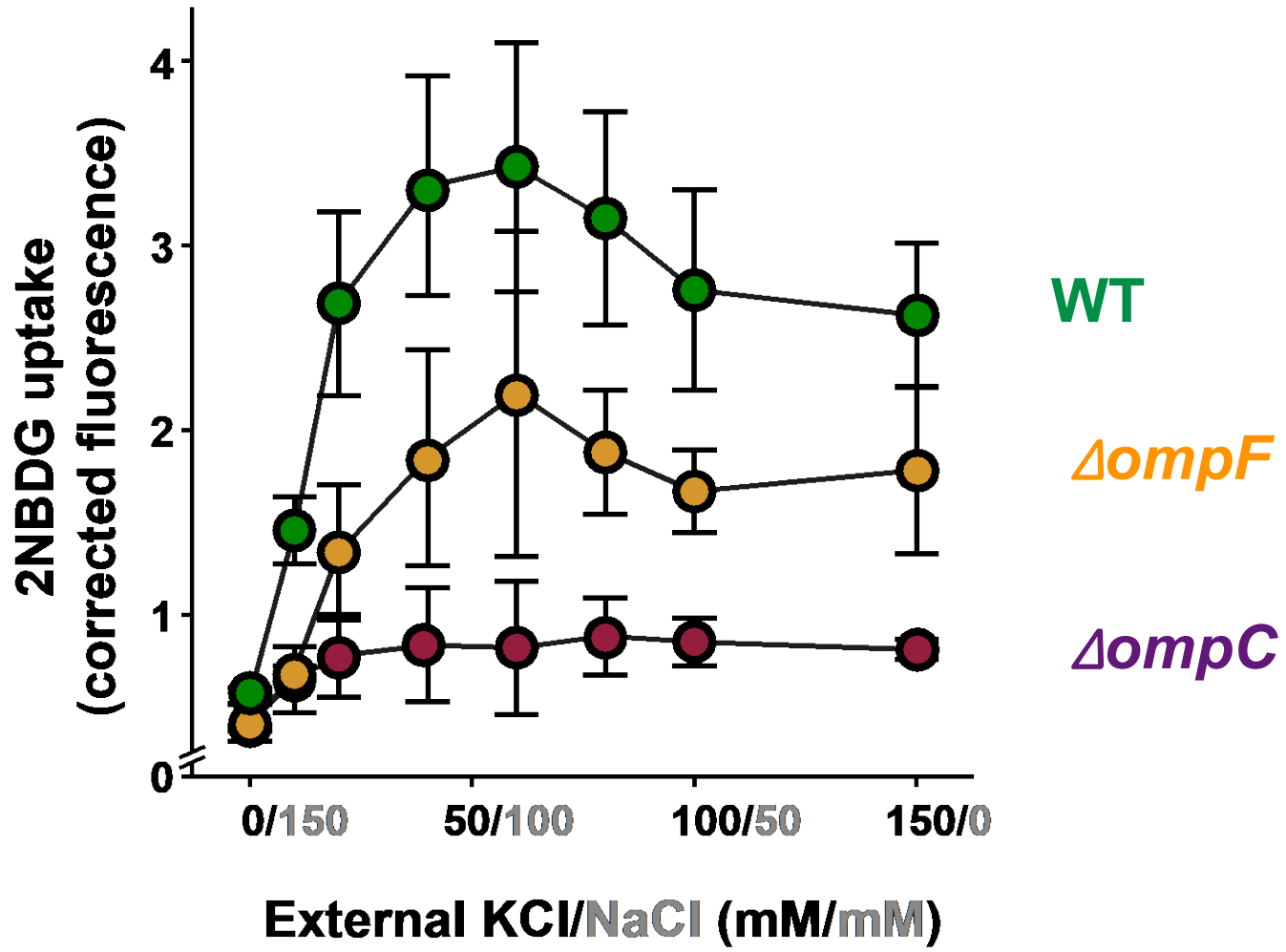
Porin permeability is regulated by internal H+



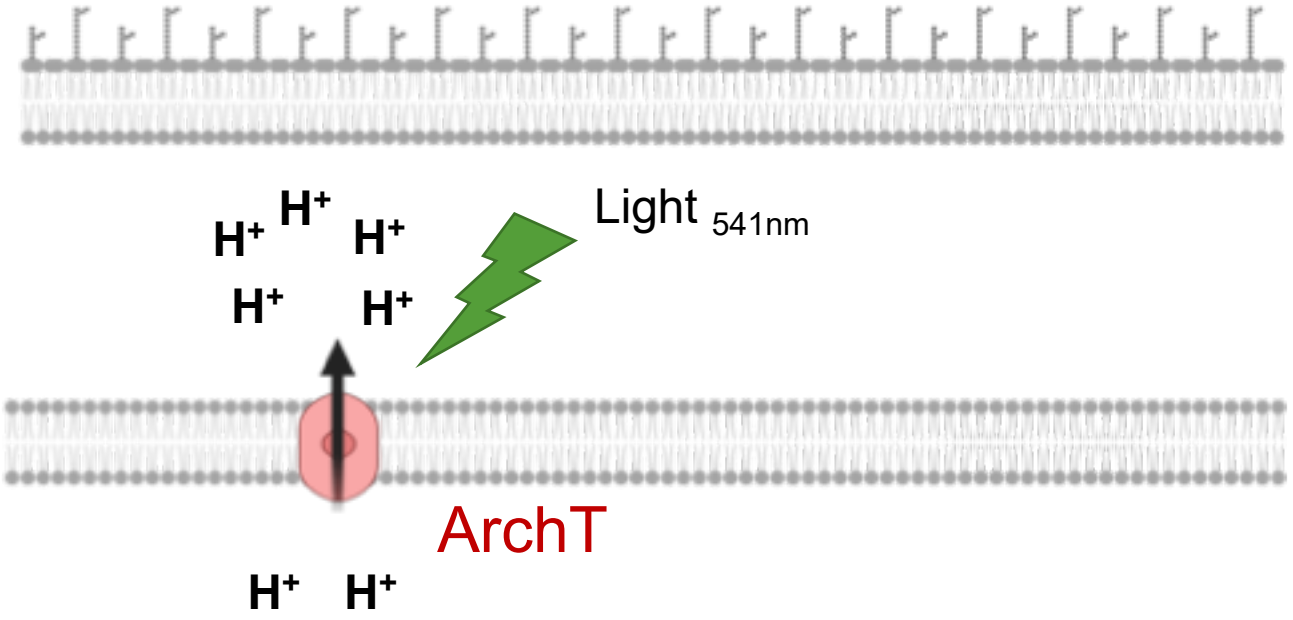
Porin permeability is regulated by internal K+

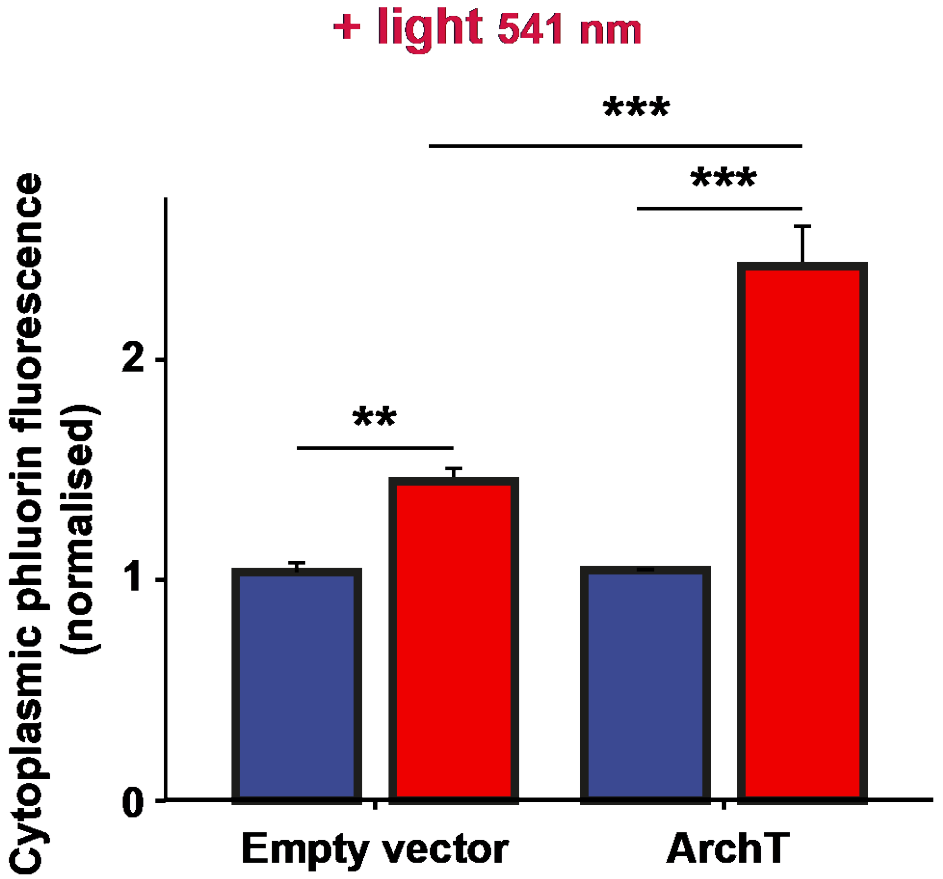


Porin permeability is regulated by internal K+



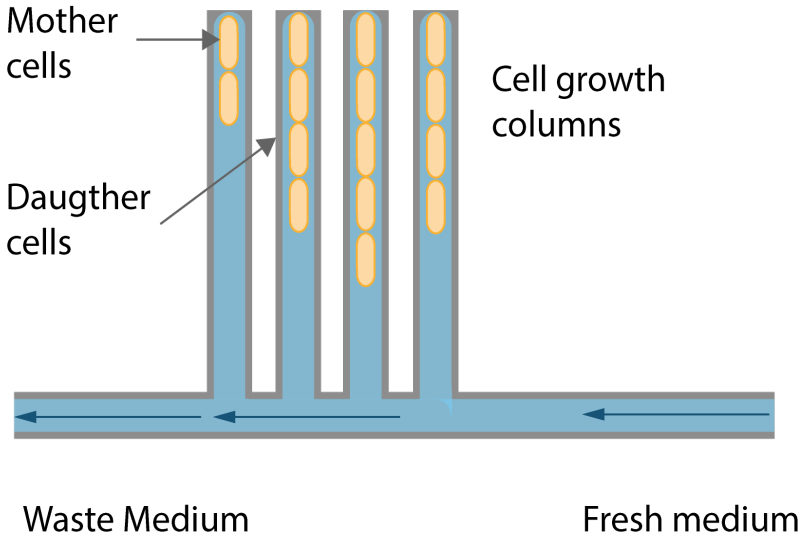
Testing the hypothesis: independent regulation of periplasmic H+

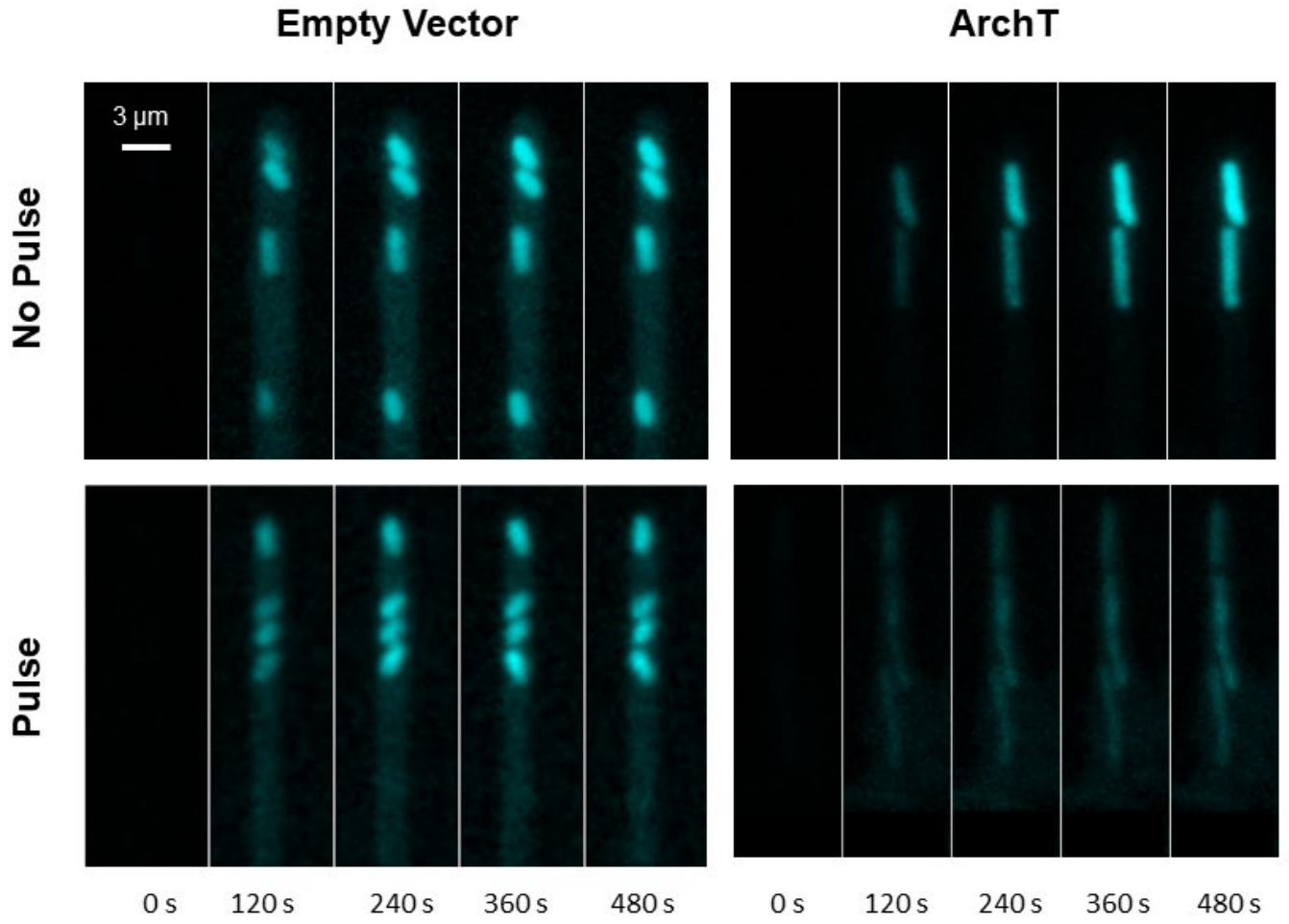




Increasing periplasmic H^+ reduces porin permeability

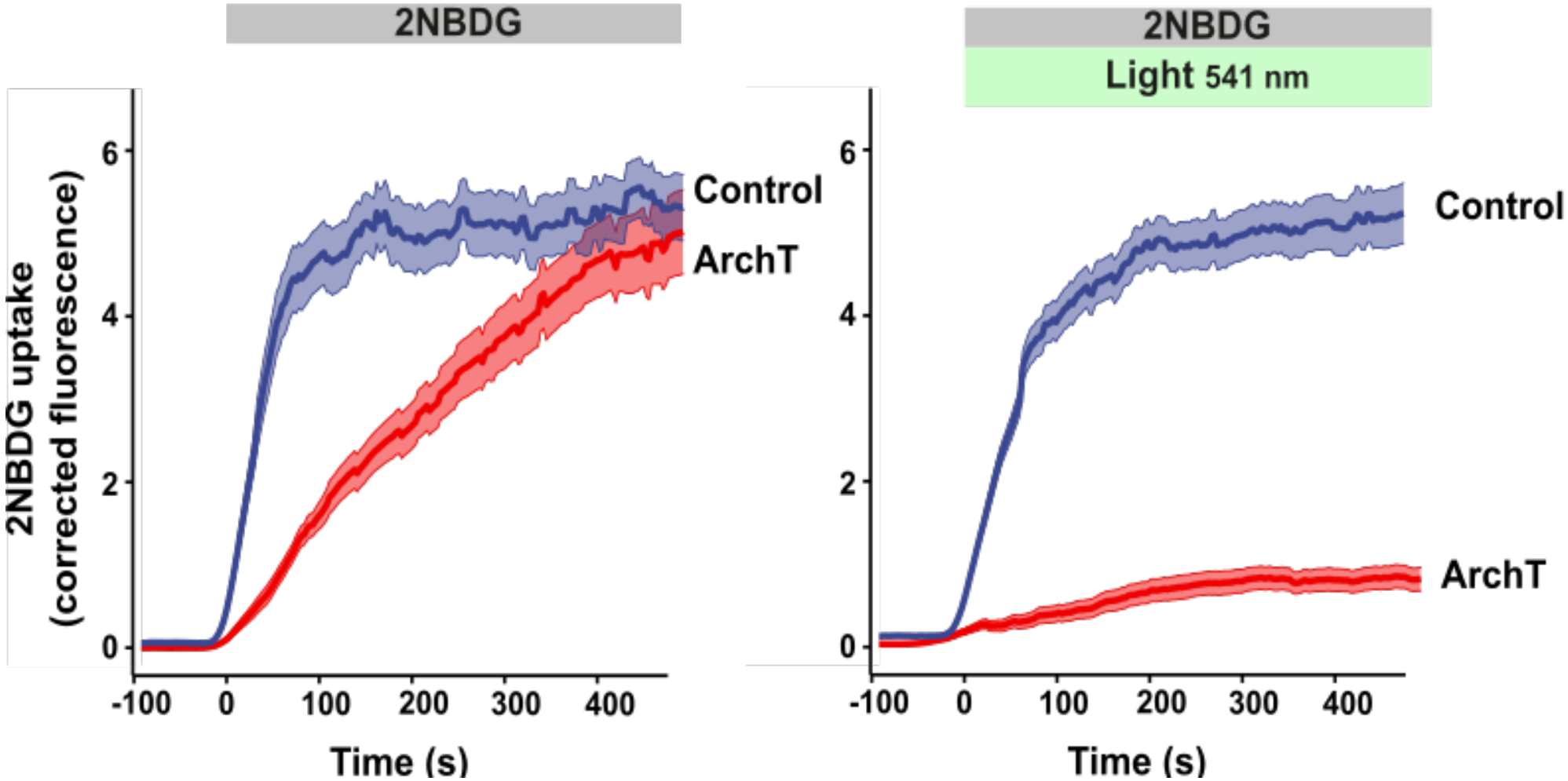
2NBDG uptake



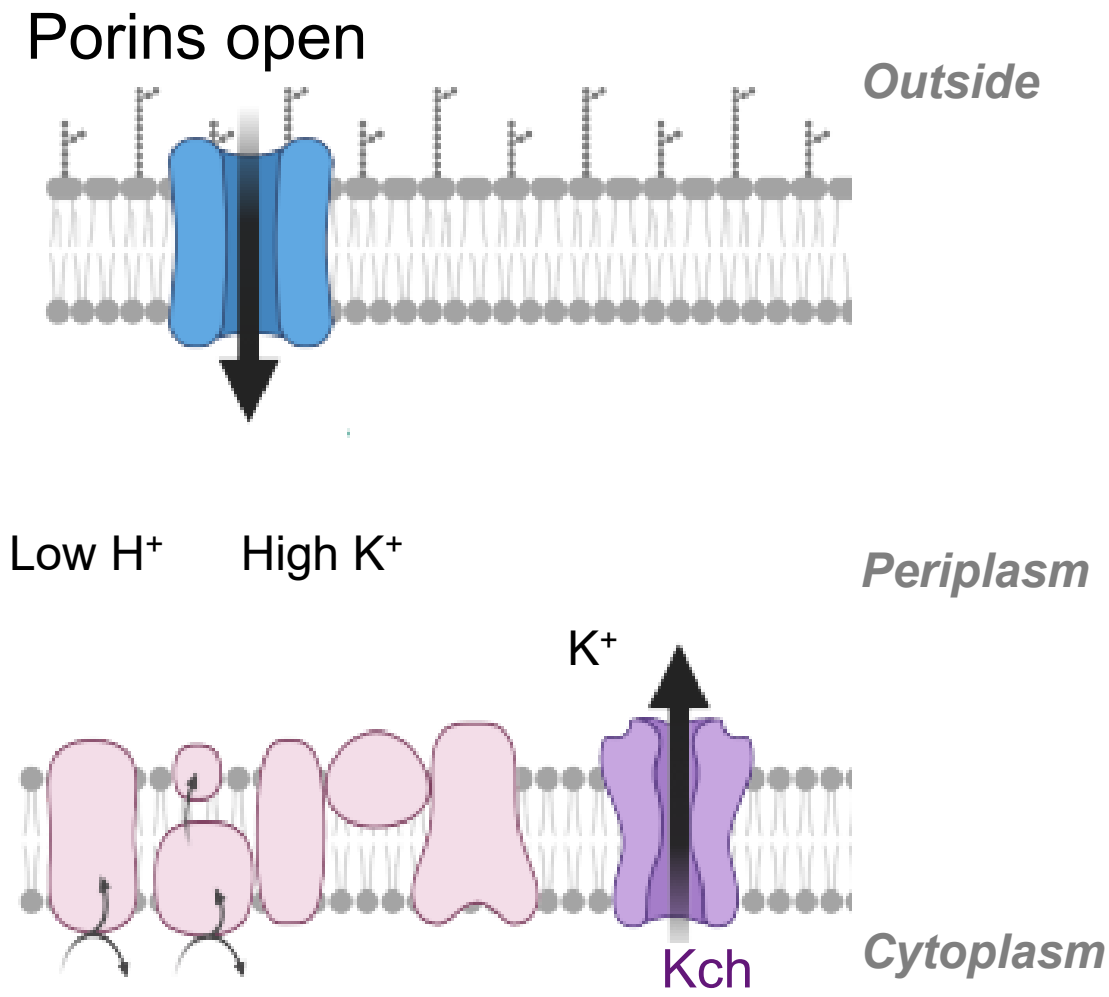


Jun Suckjoon, 2010

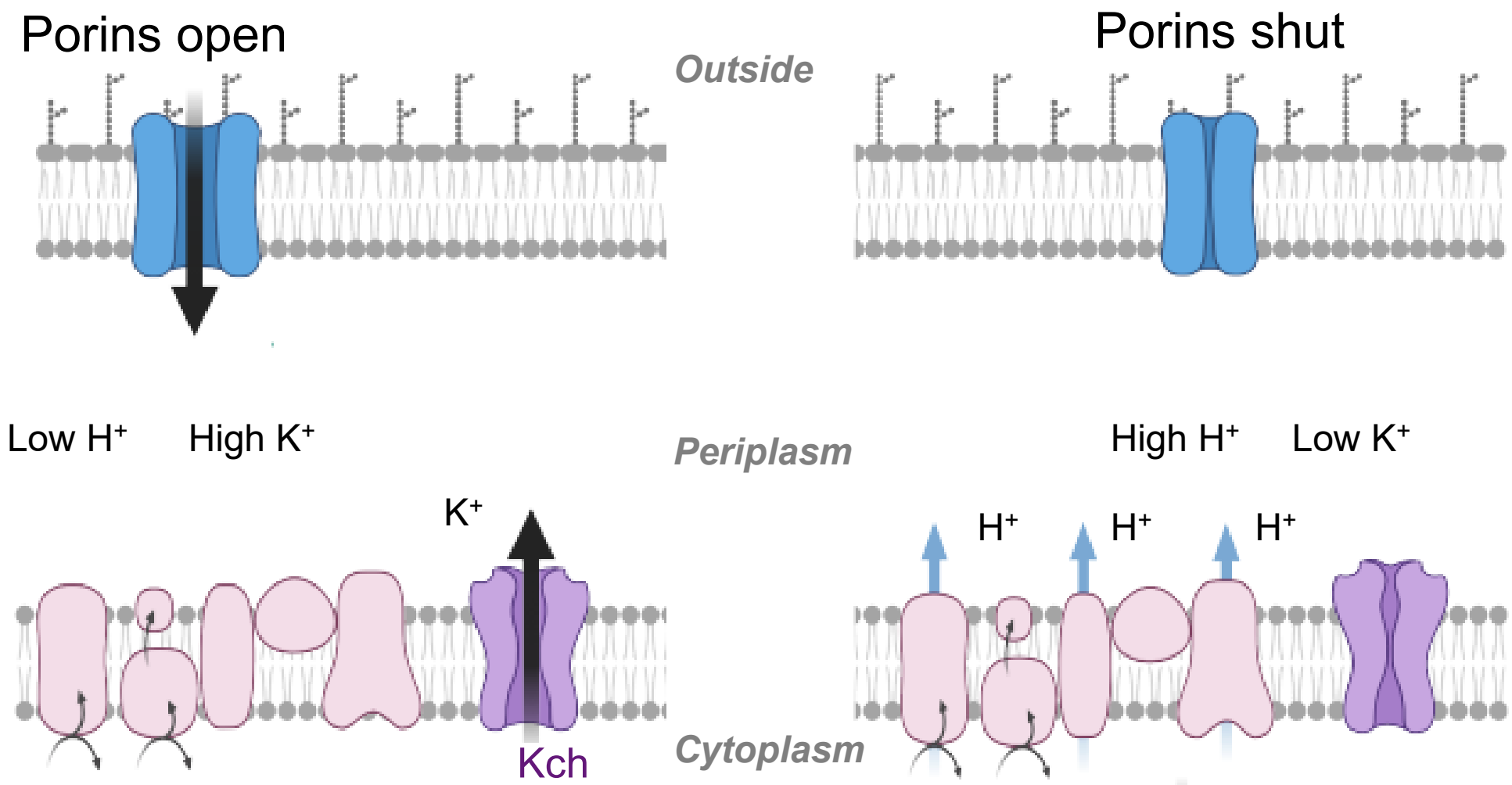
Increasing periplasmic H^+ reduces porin permeability



A model for how bacteria control porin opening

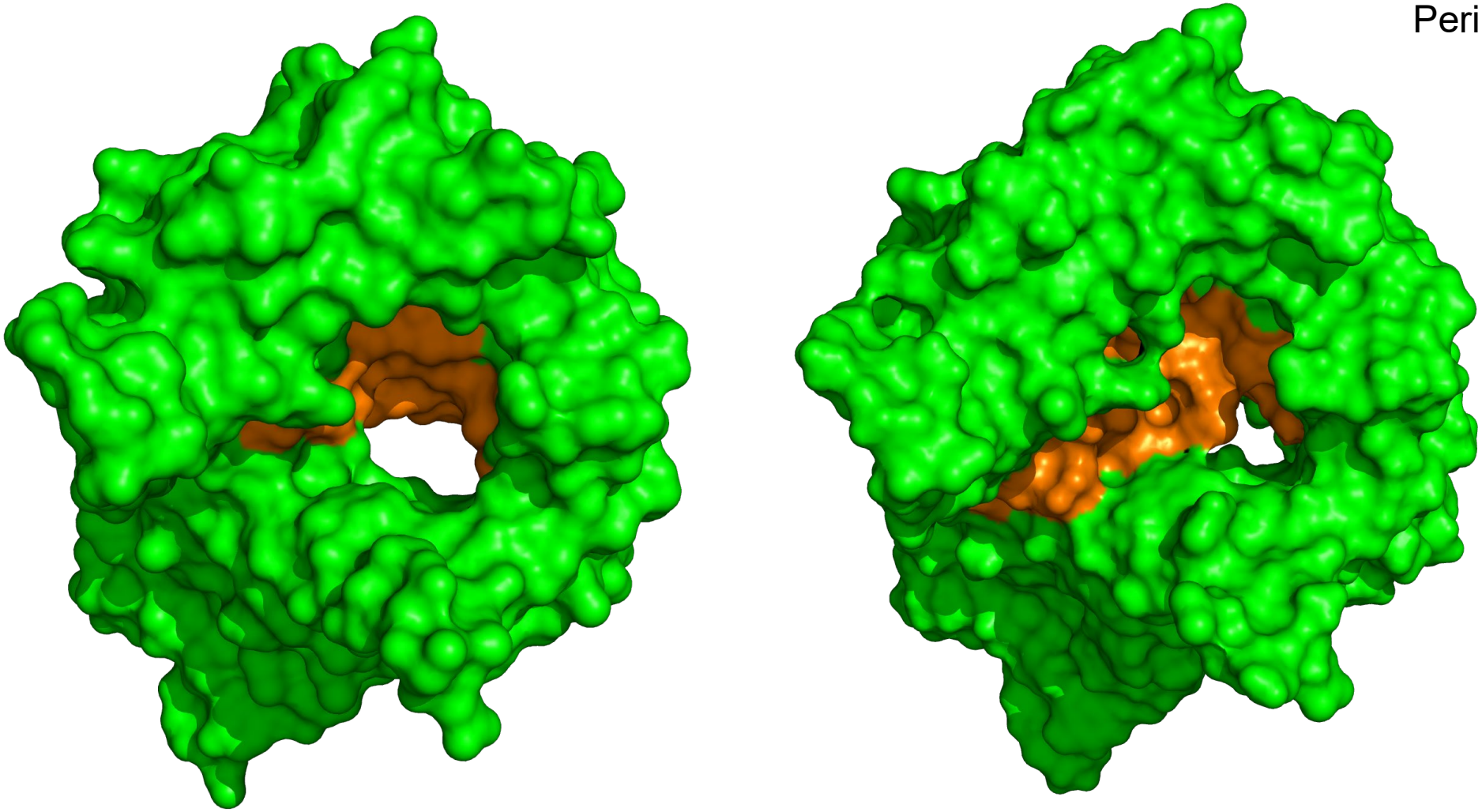


A model for how bacteria control porin opening



Structural modelling suggests periplasmic H^+ may regulate pore size

Periplasmic surface



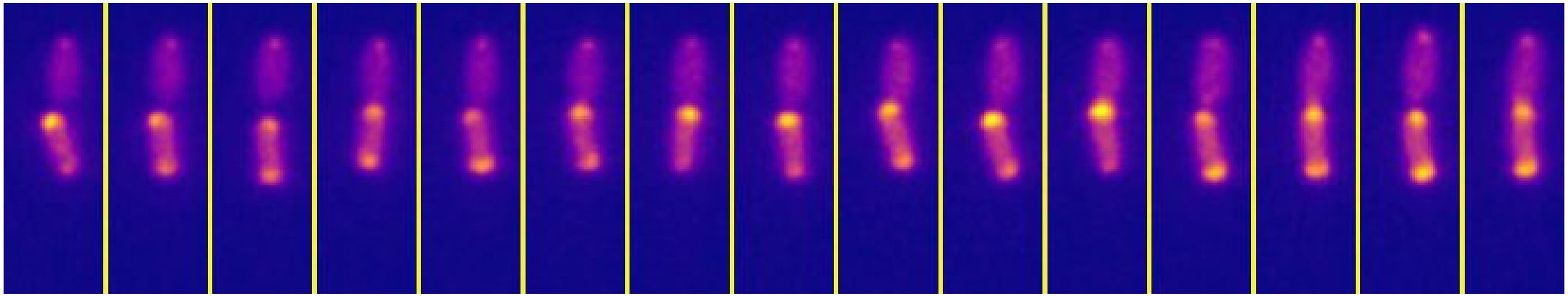
Low periplasmic H^+

High periplasmic H^+

Ali Alsulami
Tom Blundell

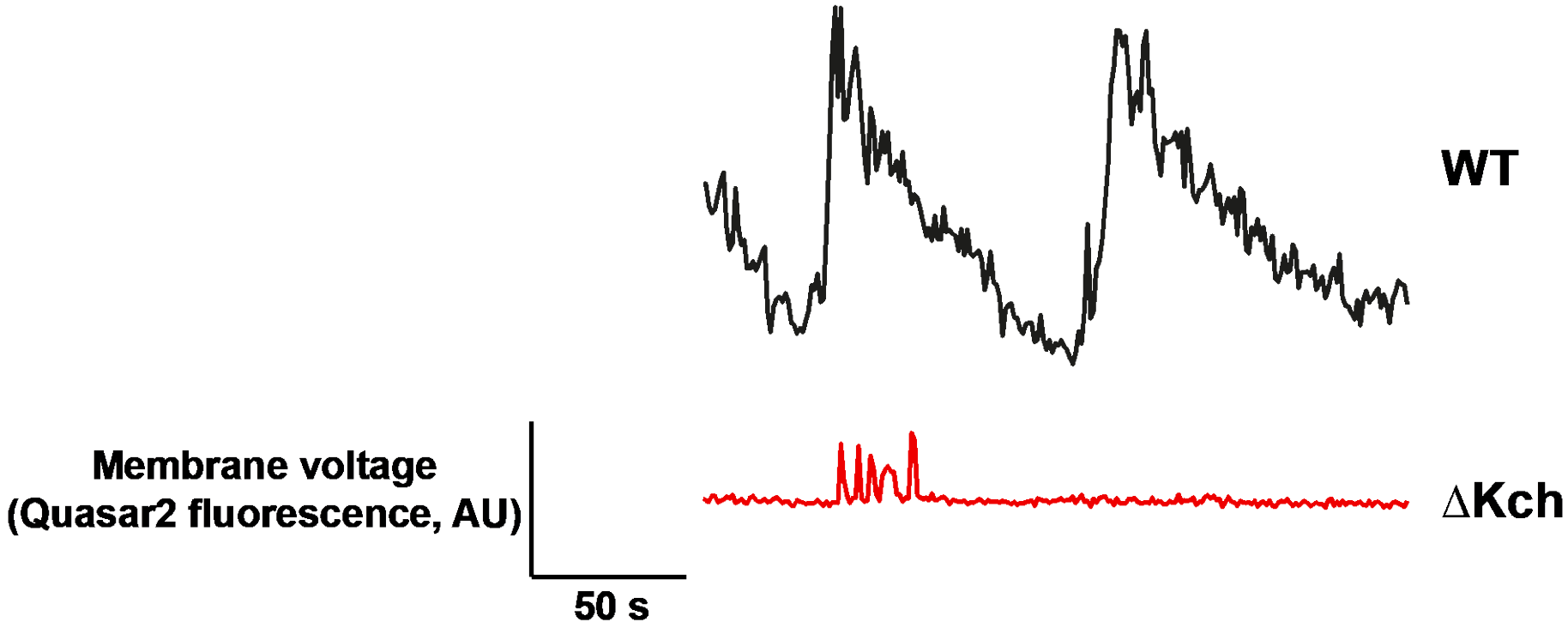
Dynamic changes in periplasmic H^+ and K^+

E. coli expressing periplasmic pH sensor (pelBC::pHuji)

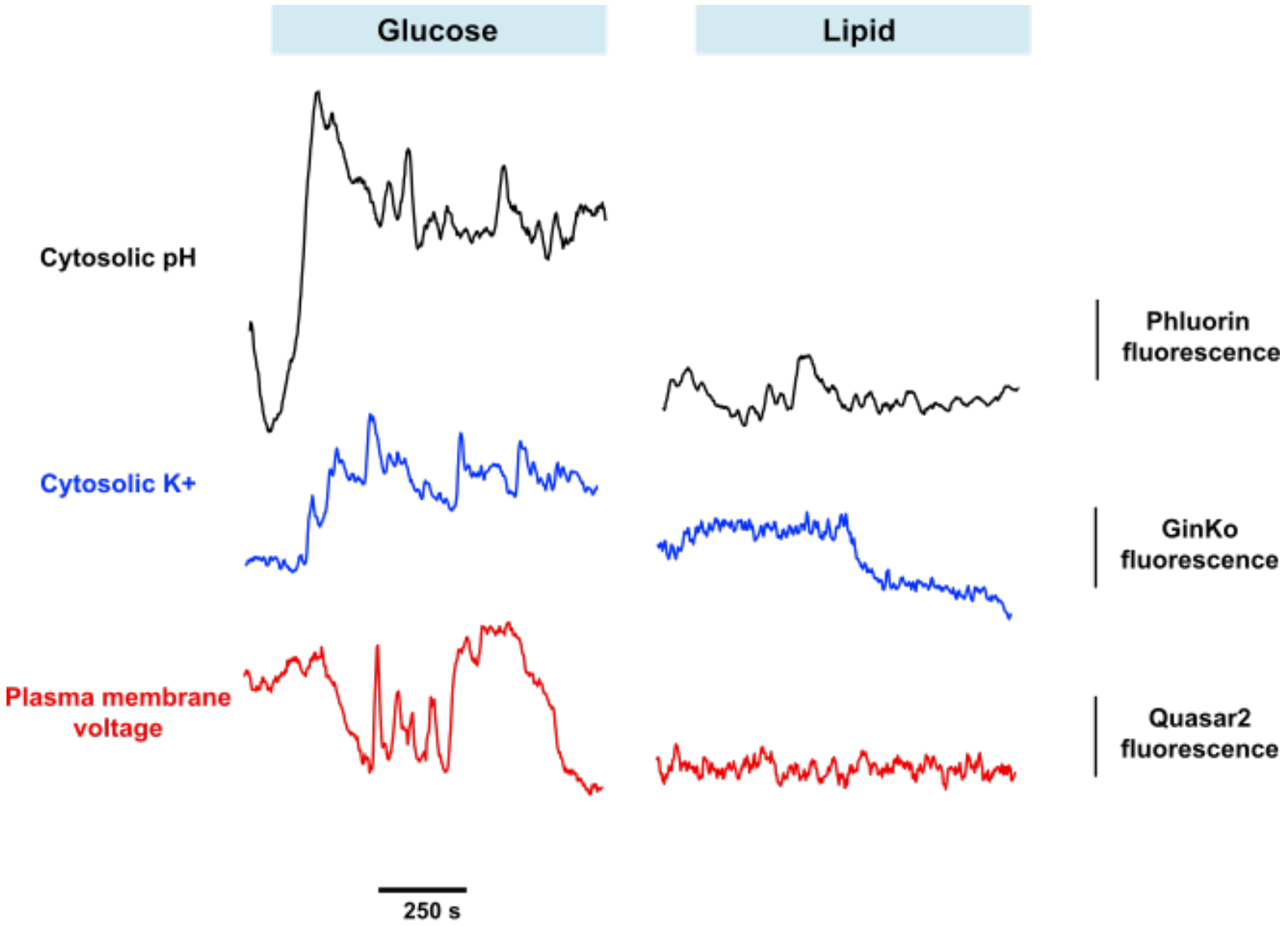


Dynamic changes in plasma membrane voltage

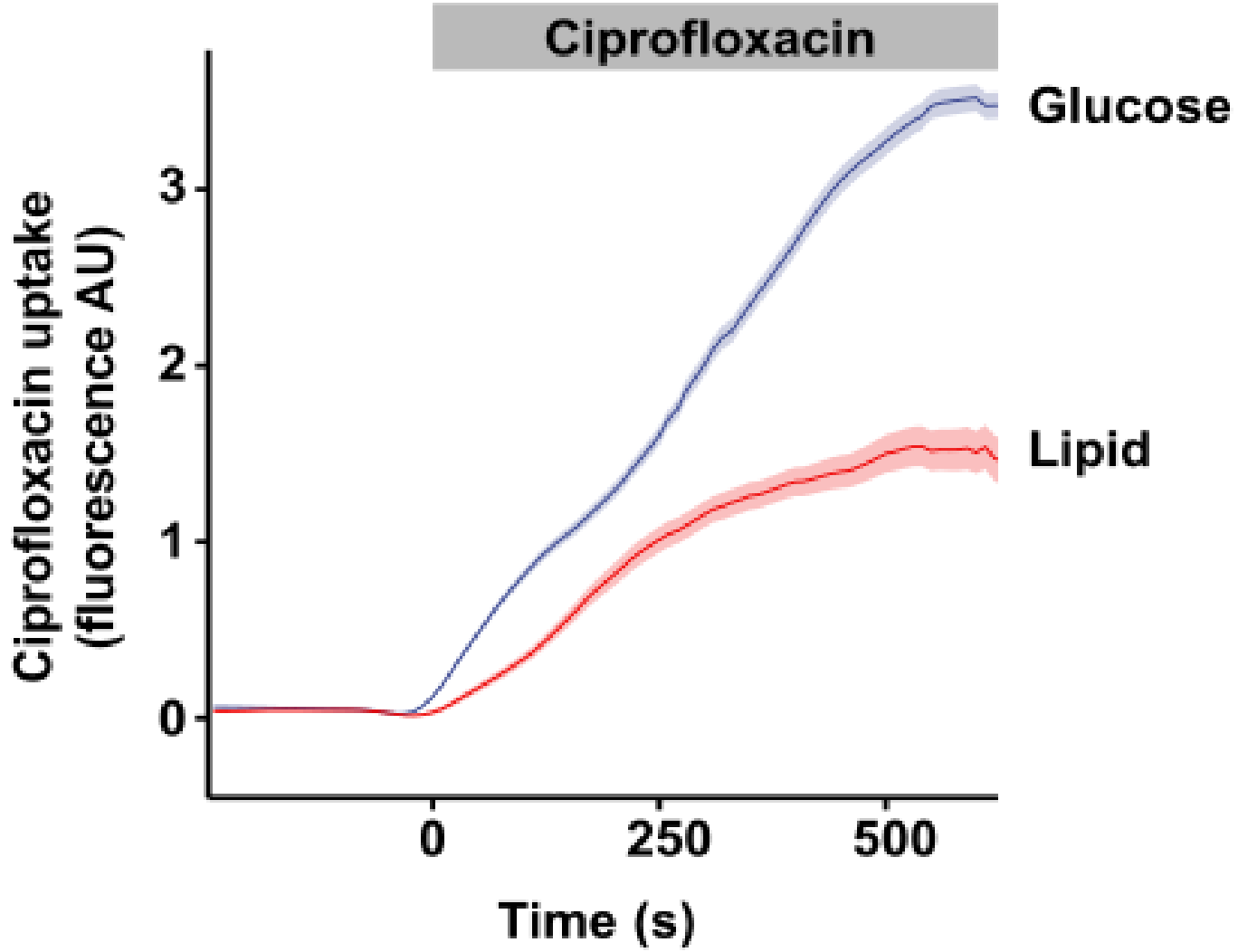
'Action potentials' driven by voltage gated K+ channel (Kch)



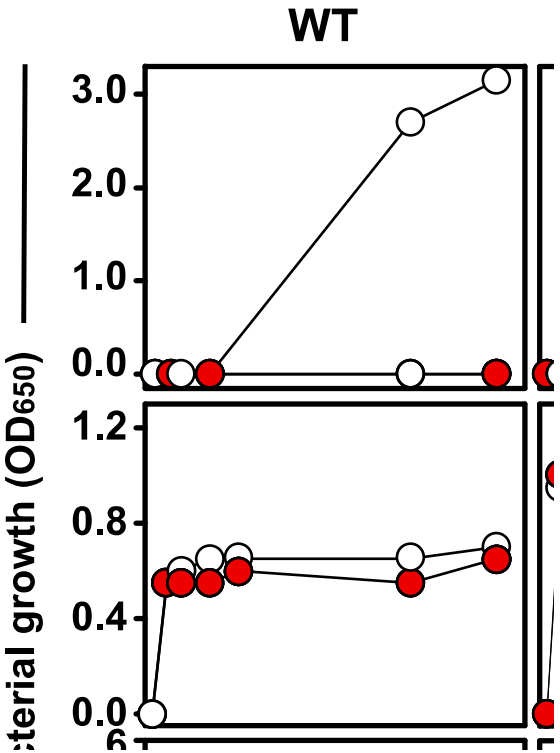
Periplasmic H+ and K+ oscillations depend on carbon source



Lipid carbon source reduce porin permeability



Lipid carbon source cause increased antibiotic resistance



Dr Ieuan Evans

Conclusions

1. Porin permeability is regulated by **periplasmic H+ and K+**

    Role of other ion channels?

    Are there spatial gradients in bacteria?

2. Structural modelling suggests that regulation may be **porin-intrinsic**

    Liposomal reconstitution experiments are underway

3. Changes in periplasmic H+ and K+ may explain different permeability and antibiotic resistance seen in lipid-eating bacteria

    What happens inside macrophages?