

Granger-causality inference of live cell movies to study actin regulation for cell motility

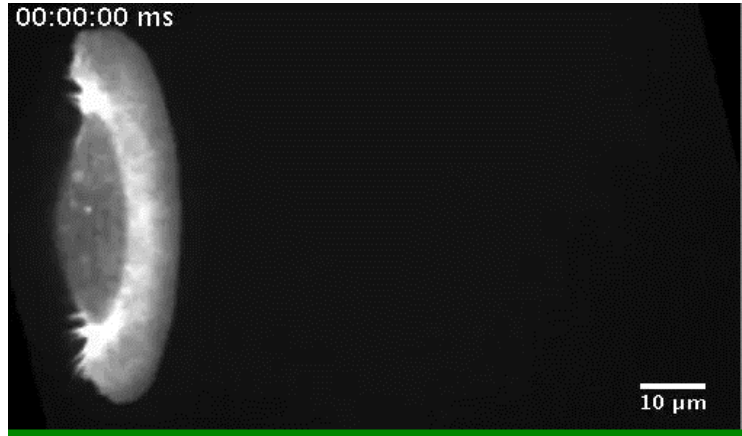
April, 2021

Jungsik Noh

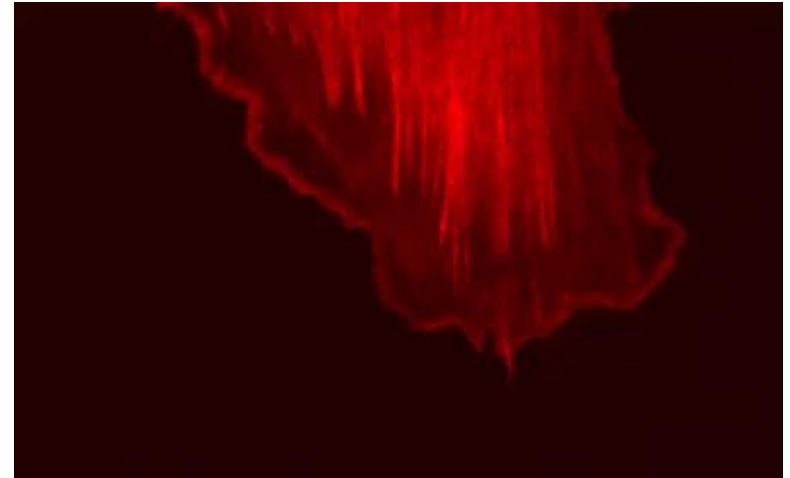
Lyda Hill Department of Bioinformatics

Dynamic lamellipodia at the migrating cell edge

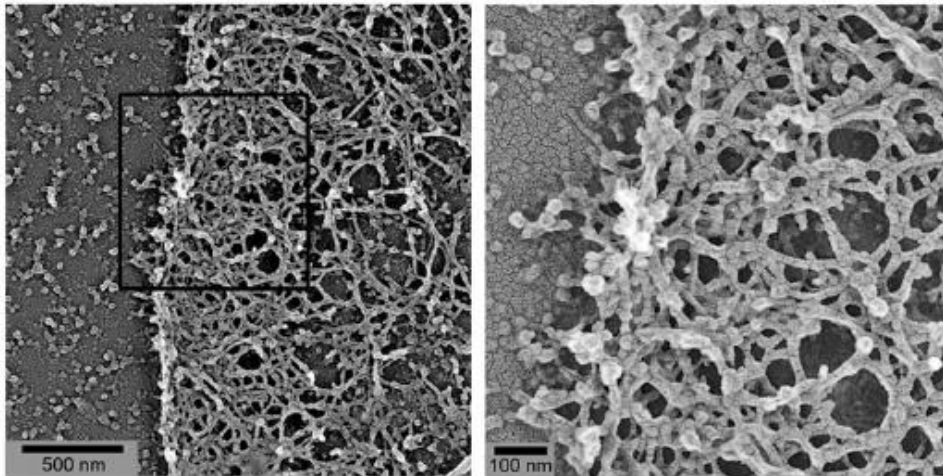
Actin in a keratocyte migrating on 2D



Actin in a human bone cancer cell (U2OS)

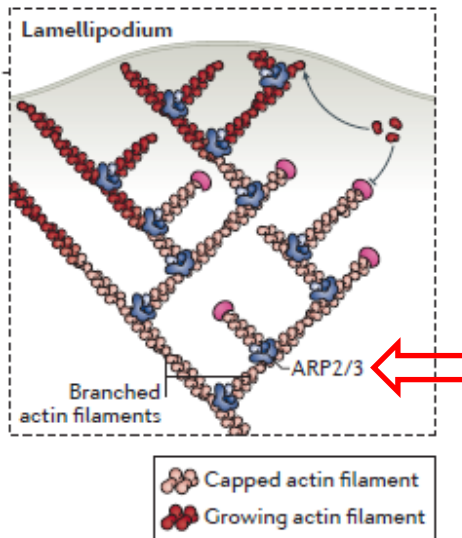


Lamellipodium is a actin-rich motile structure at the cell edge

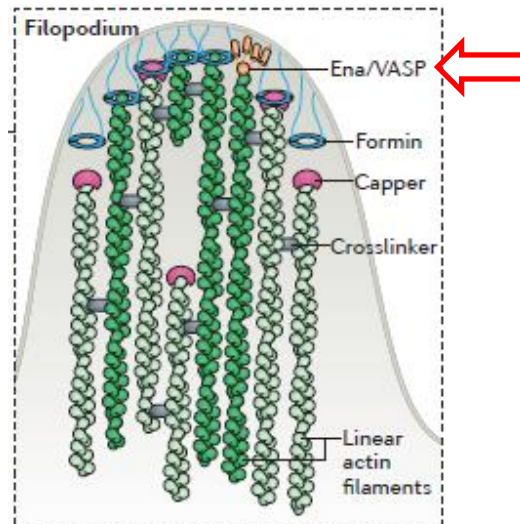


Actin filaments regulation

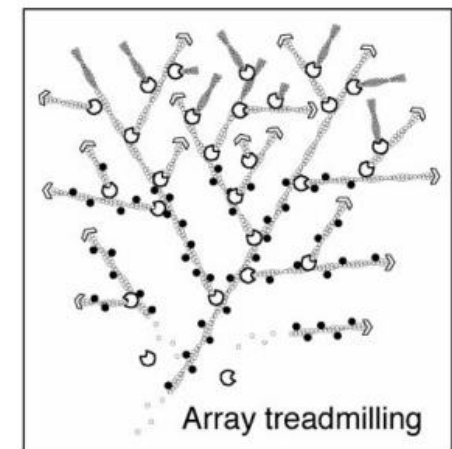
- Branching



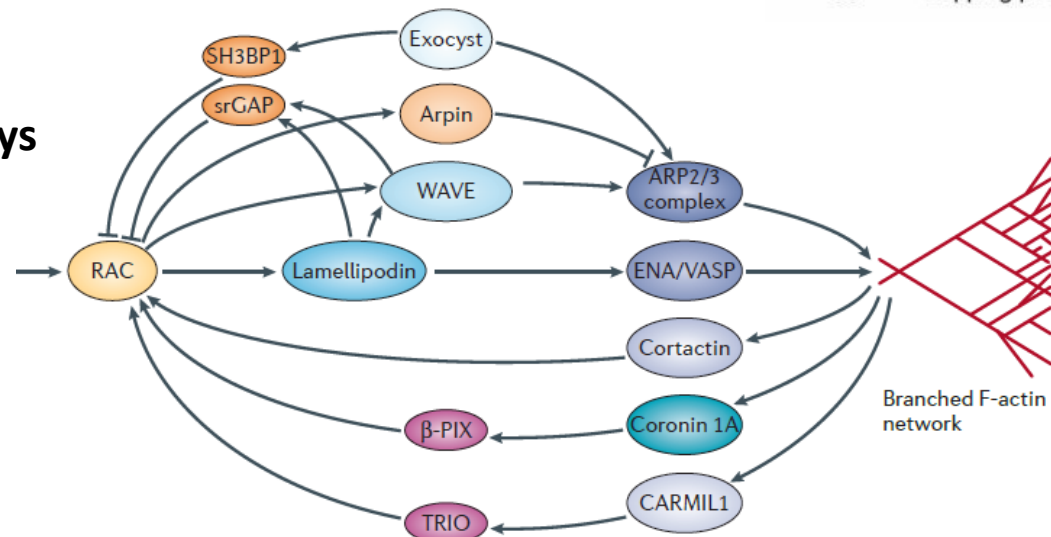
- Elongation/Capping



- Debranching and severing



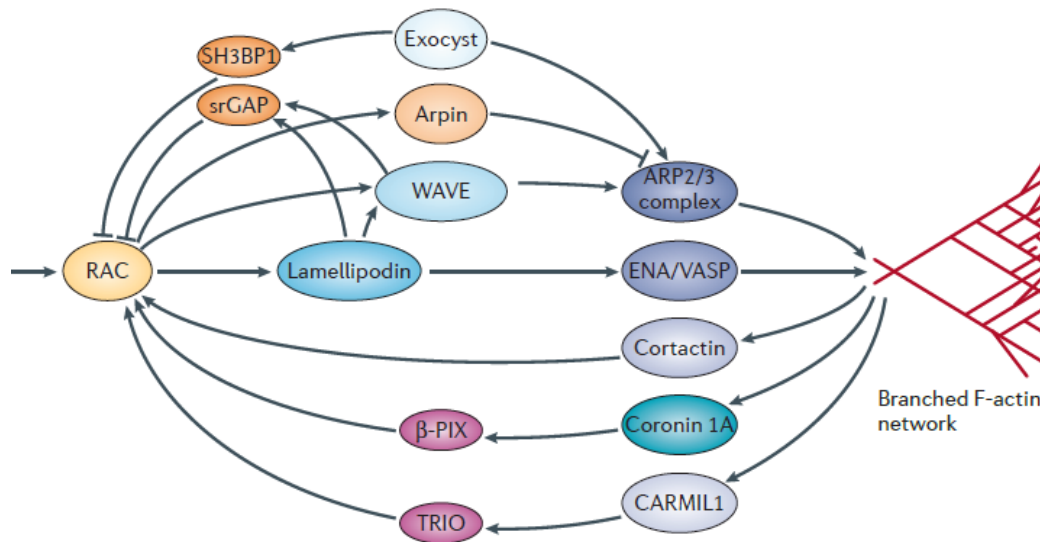
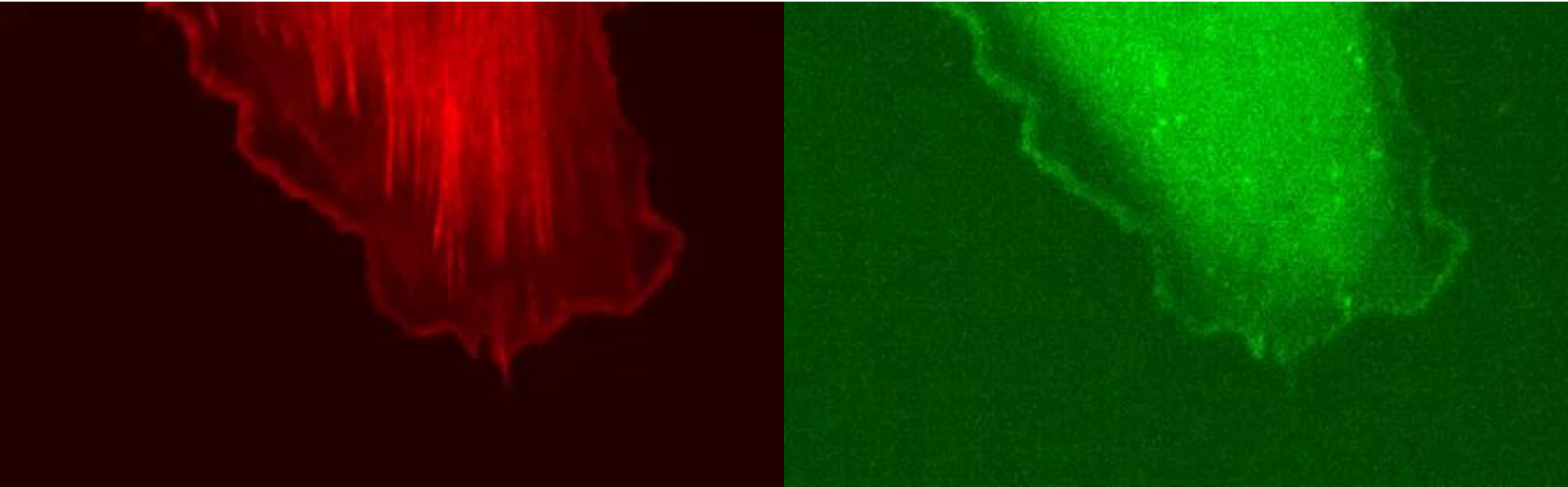
Actin regulatory pathways equipped with feedback loops



Live cell fluorescence imaging

Actin

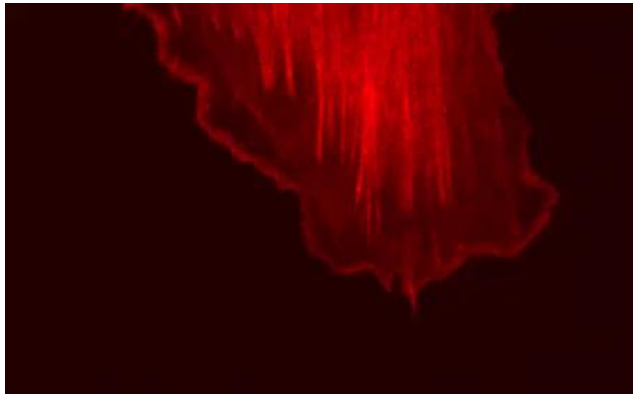
Arp2/3



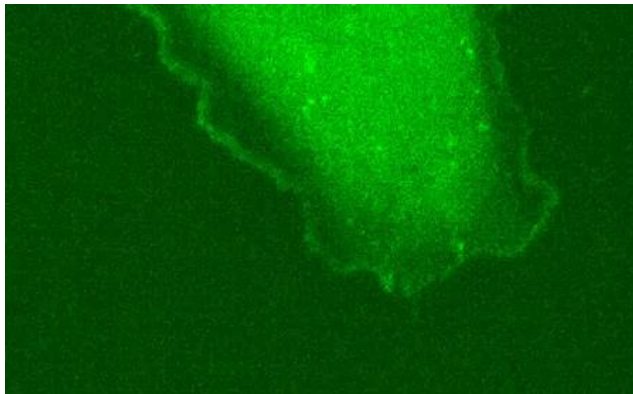
Can we infer causal pathways between proteins from live cell images?

Live cell fluorescence imaging + image processing

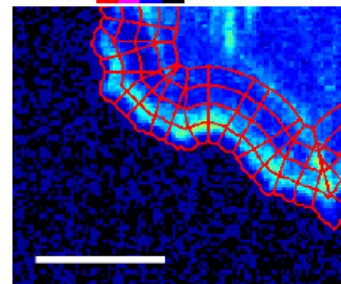
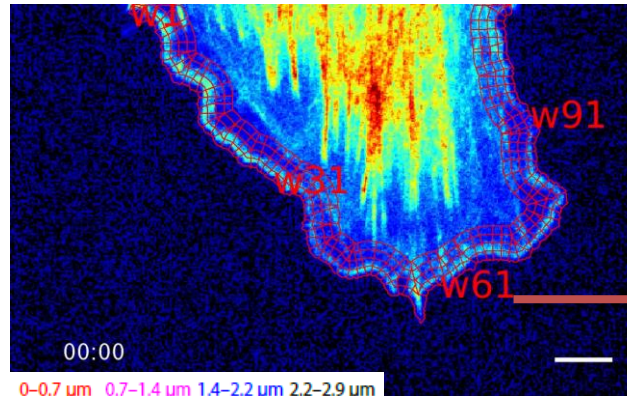
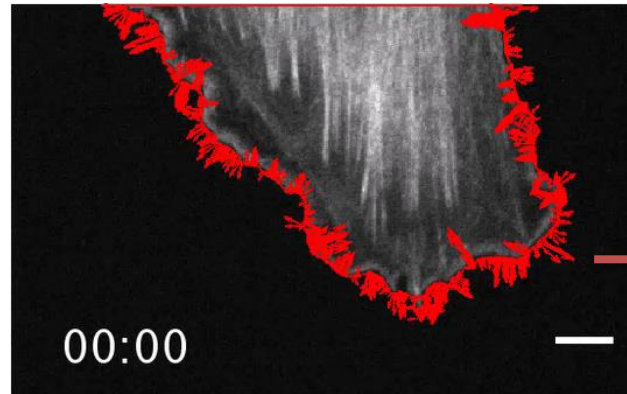
Actin



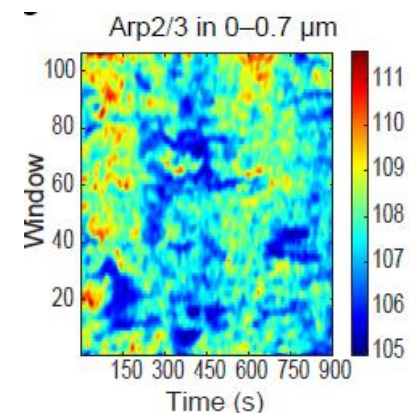
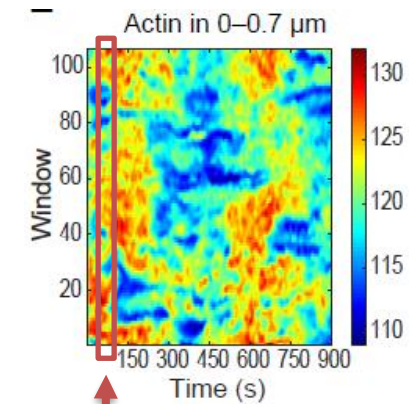
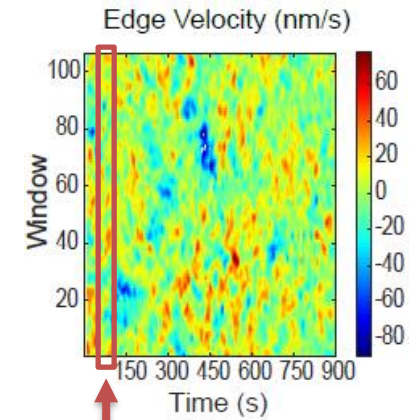
Arp2/3



Tracking cell shape changes



Scale bar:
5 μm

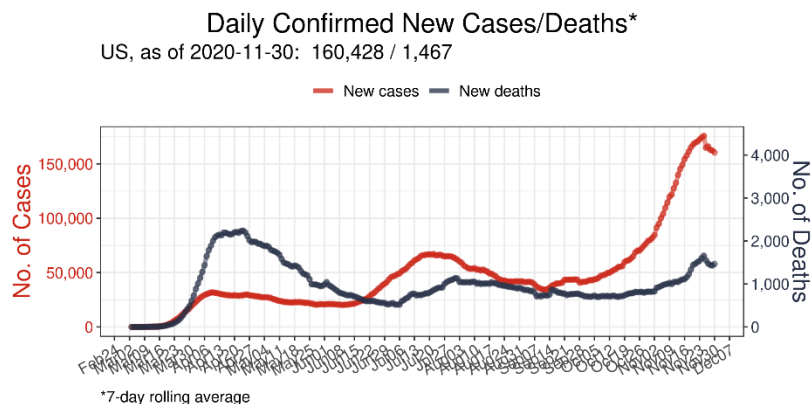


*Machacek and Danuser (2006)

*Machacek et al. (2009)

Live cell fluorescence imaging + image processing + statistical causal inference

Cause-effect relation

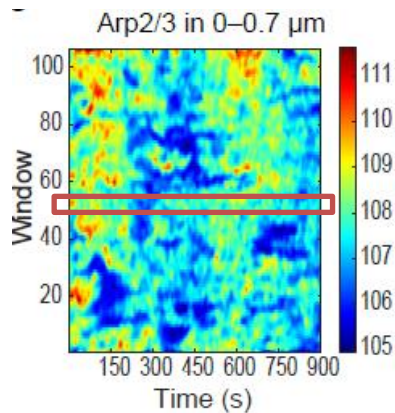


- Covid infections **cause** Covid deaths.
- Covid deaths **do not cause** Covid infections.

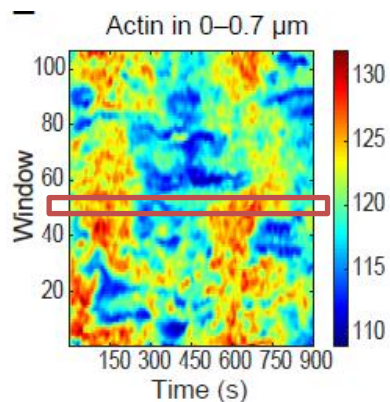
Granger-Causality (Granger, 1969) for time series (TS)

- Statistically testable definition of causality between economic time series
- TS of Covid infections is said to **Granger-cause** TS of Covid deaths, if
the prediction of Covid deaths **using** the information including Covid infections
>> the prediction of Covid deaths **without using** Covid infections

Granger-Causality (GC) test at a single window



Does
Arp2/3
cause
actin?



Full Model

Current actin in a window

Plasma-membrane
0–0.7 μm
0.7–1.4 μm
1.4–2.2 μm

Past actin in the
same and adjacent
windows

Arp2/3 until the
present time in the
same and adjacent
windows

Edge velocity until
the present time

vs. Reduced Model

Current actin in a window

Past actin in the
same and adjacent
windows

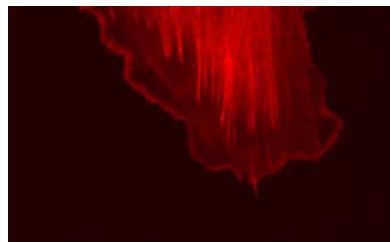
Arp2/3 until the
present time
except the same
window

Edge velocity until
the present time

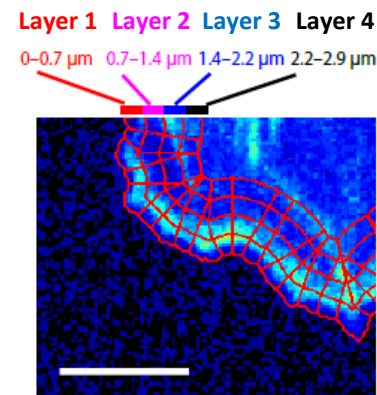
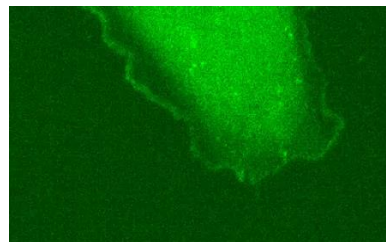
If **Full Model** \gg **Reduced Model**, Arp2/3 \rightarrow Actin in the window.

Subcellular causal evidences for one cell

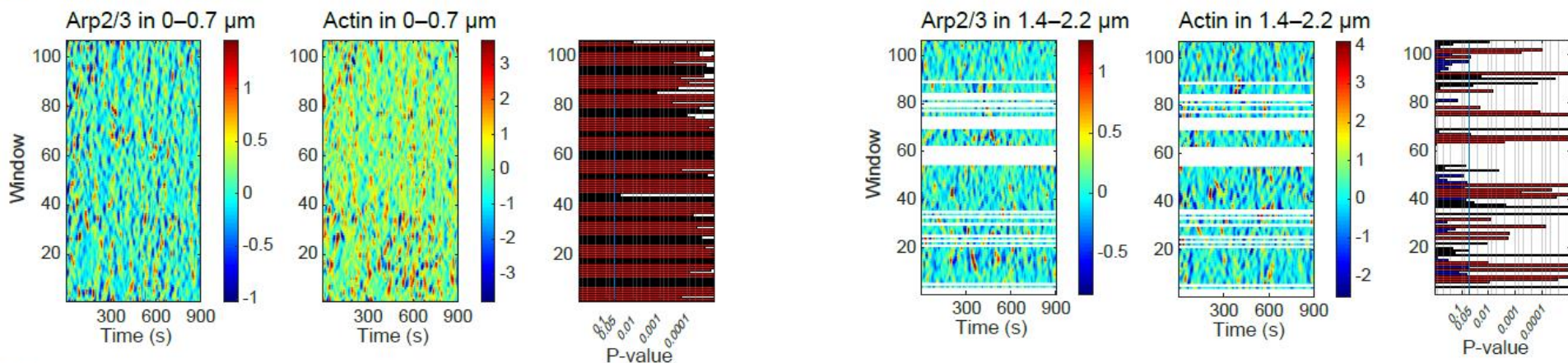
Actin



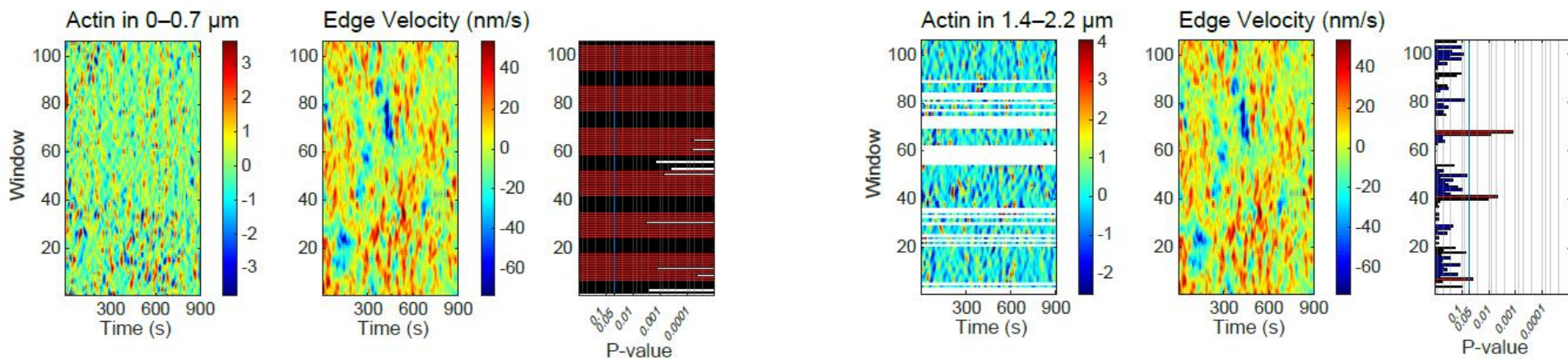
Arp2/3



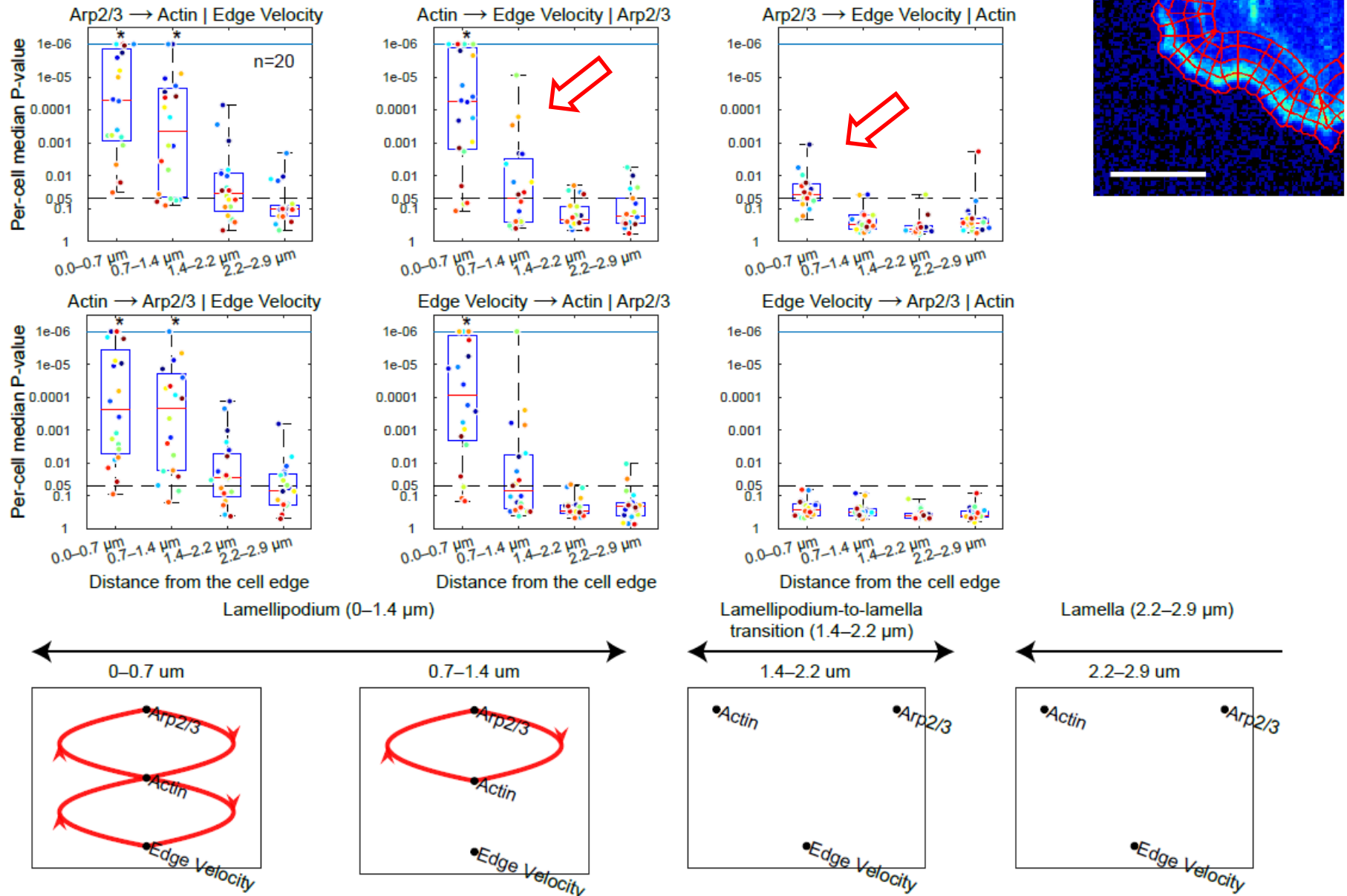
C Arp2/3 → Actin



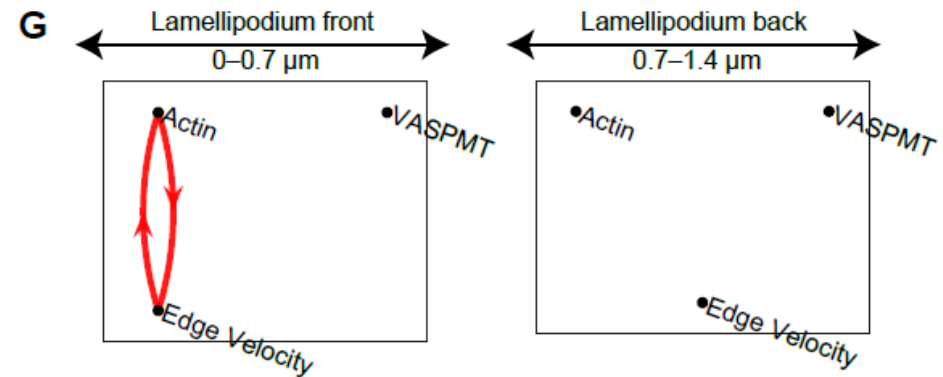
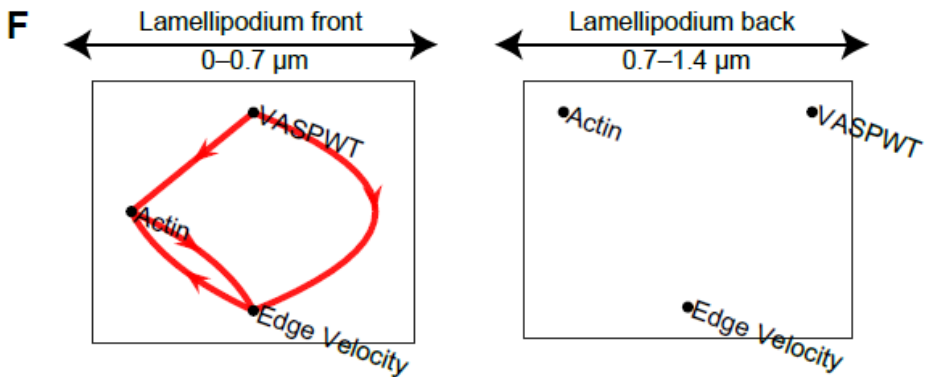
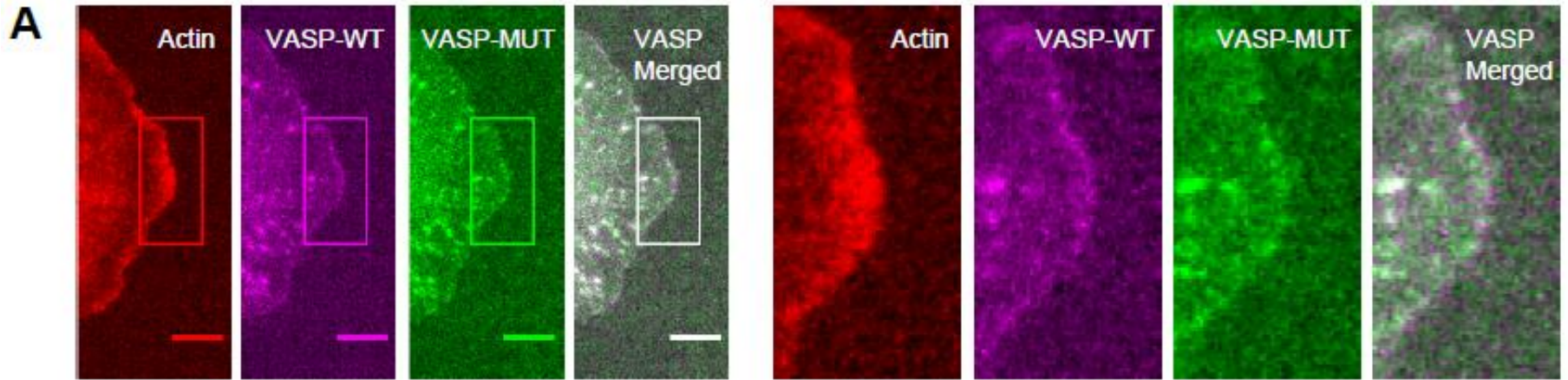
D Actin → Edge Velocity



GC evidences for multiple cells

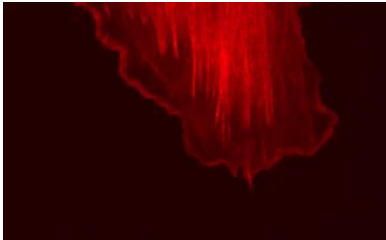


GC inference detects genetic amino acid mutations

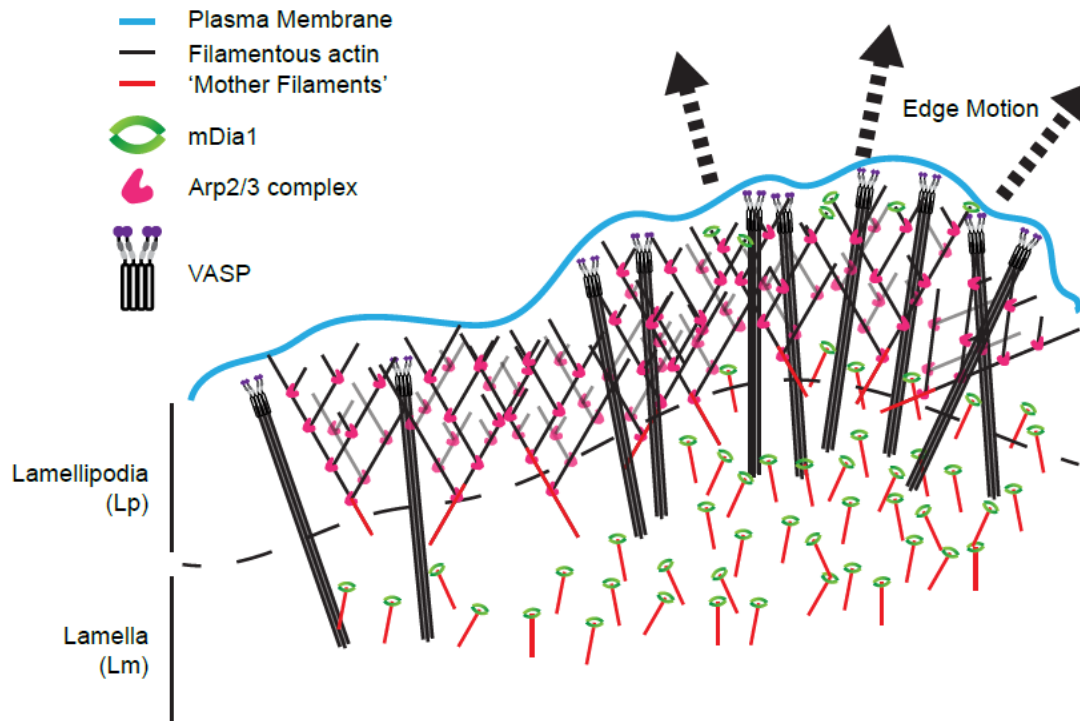
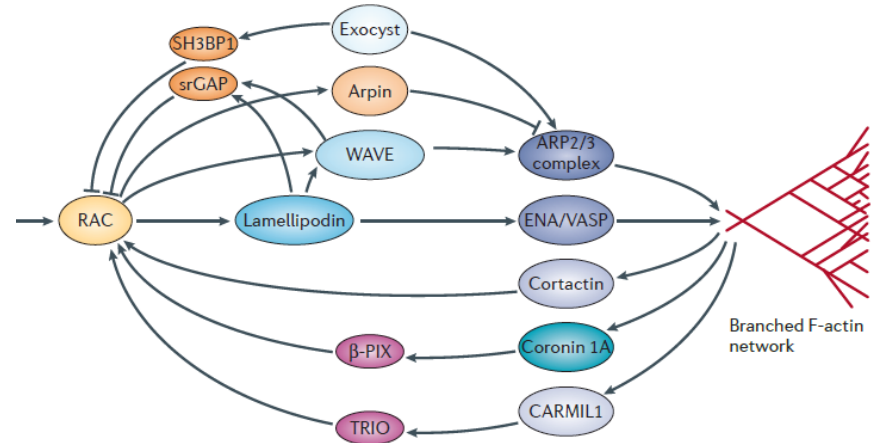
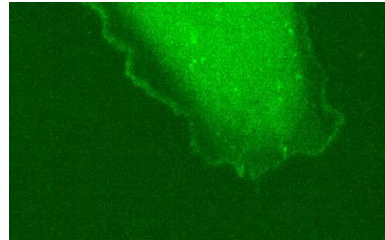


Summary

Actin



Arp2/3



Granger-causality pathway

