



OPEN SESSION

FOR INFORMATION ONLY

(No formal action is requested at this time)

1. Chair's Remarks
Julia Grumbles, UNC-CH Board of Trustees
2. Creativity Hubs
Terry Magnuson, Vice Chancellor for Research
 - UNC's Evryscope: A Watchful Eye on the Entire Sky
Nick Law, Assistant Professor, Physics & Astronomy
 - From Molecules to Organisms: Pushing the limits of
Fluorescence Microscopy
*Wesley Legant, Assistant Professor, Pharmacology and
Biomedical Engineering*

COMMITTEE MEMBERS

Julia Sprunt Grumbles, Chair
Kelly Matthews Hopkins, Vice Chair
Jefferson W. Brown
W. Lowry Caudill
Allie Ray McCullen
Hari H. Nath

Administrative Liaison:

Bob Blouin, Executive Vice Chancellor and Provost
***Judith Cone, Vice Chancellor for Innovation, Entrepreneurship, & Economic
Development***

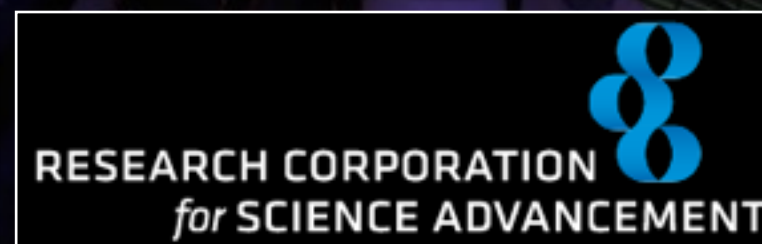
UNC's Evryscopes: Watchful Eyes on the Entire Sky

Nicholas Law

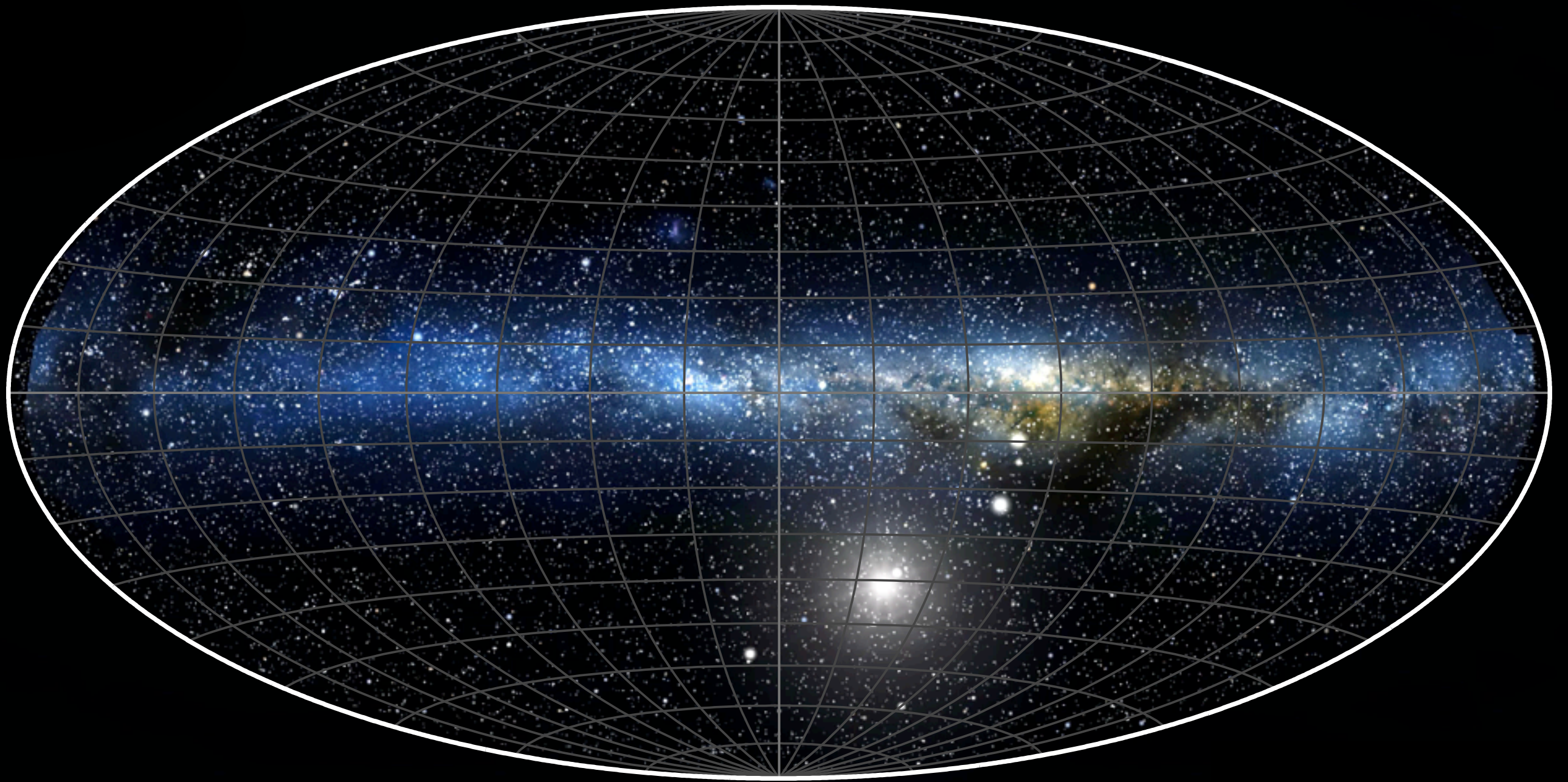
Assistant Professor

Dept. of Physics and Astronomy

University of North Carolina, Chapel Hill



The dynamic sky



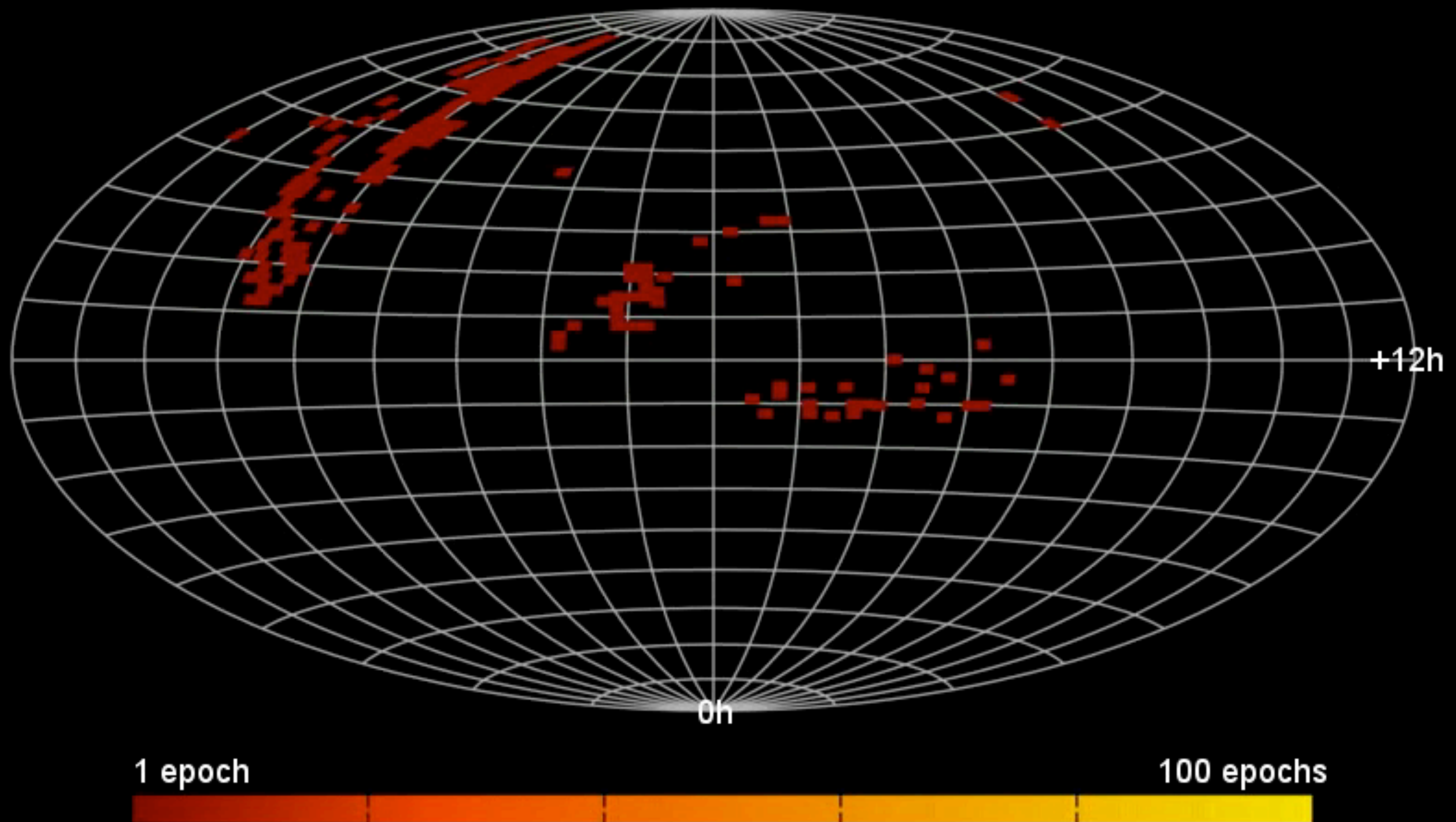
Standard sky surveys: tiling across the sky



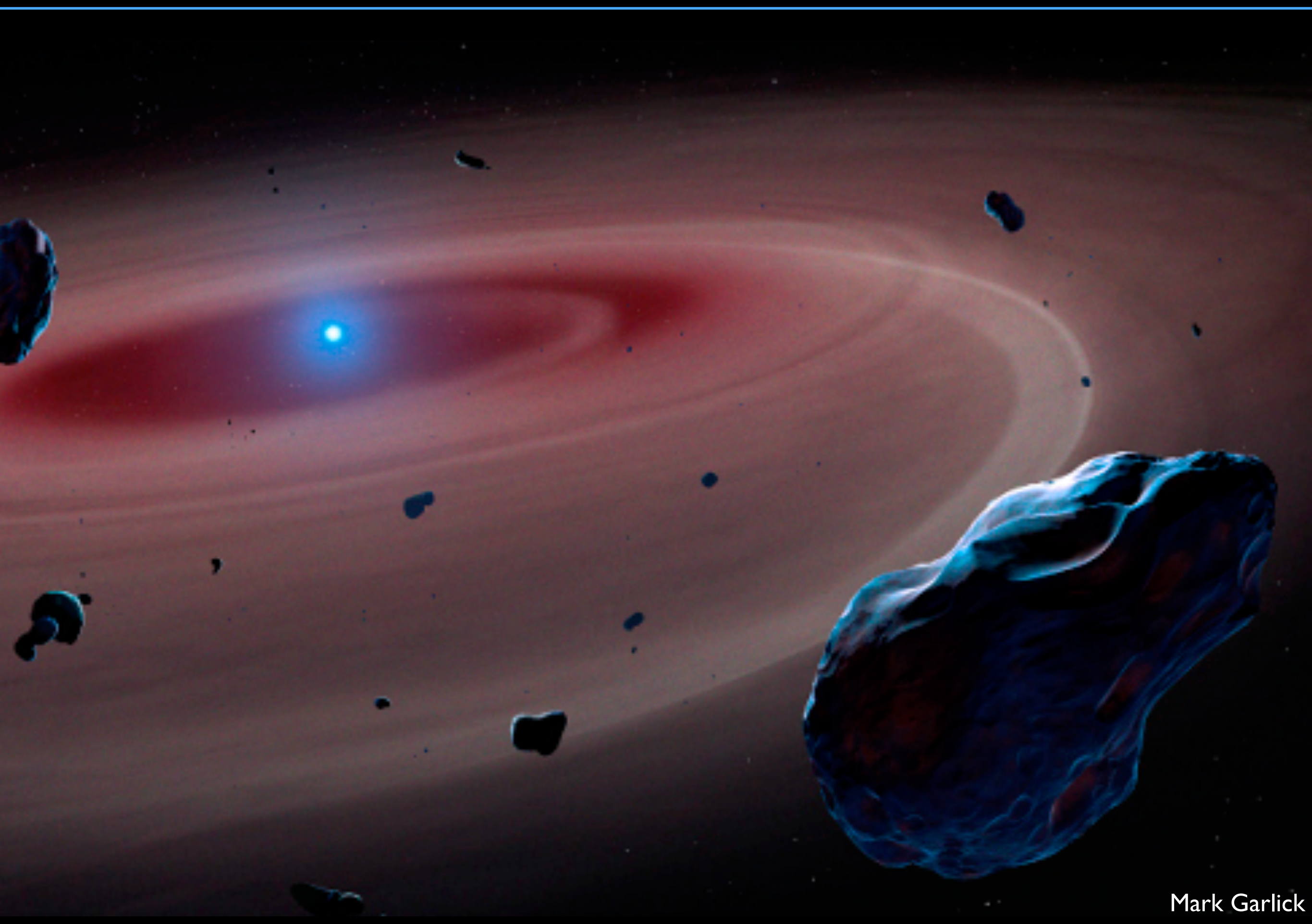
PTF supernova survey: Law et al. 2009

Standard sky surveys: tiling across the sky

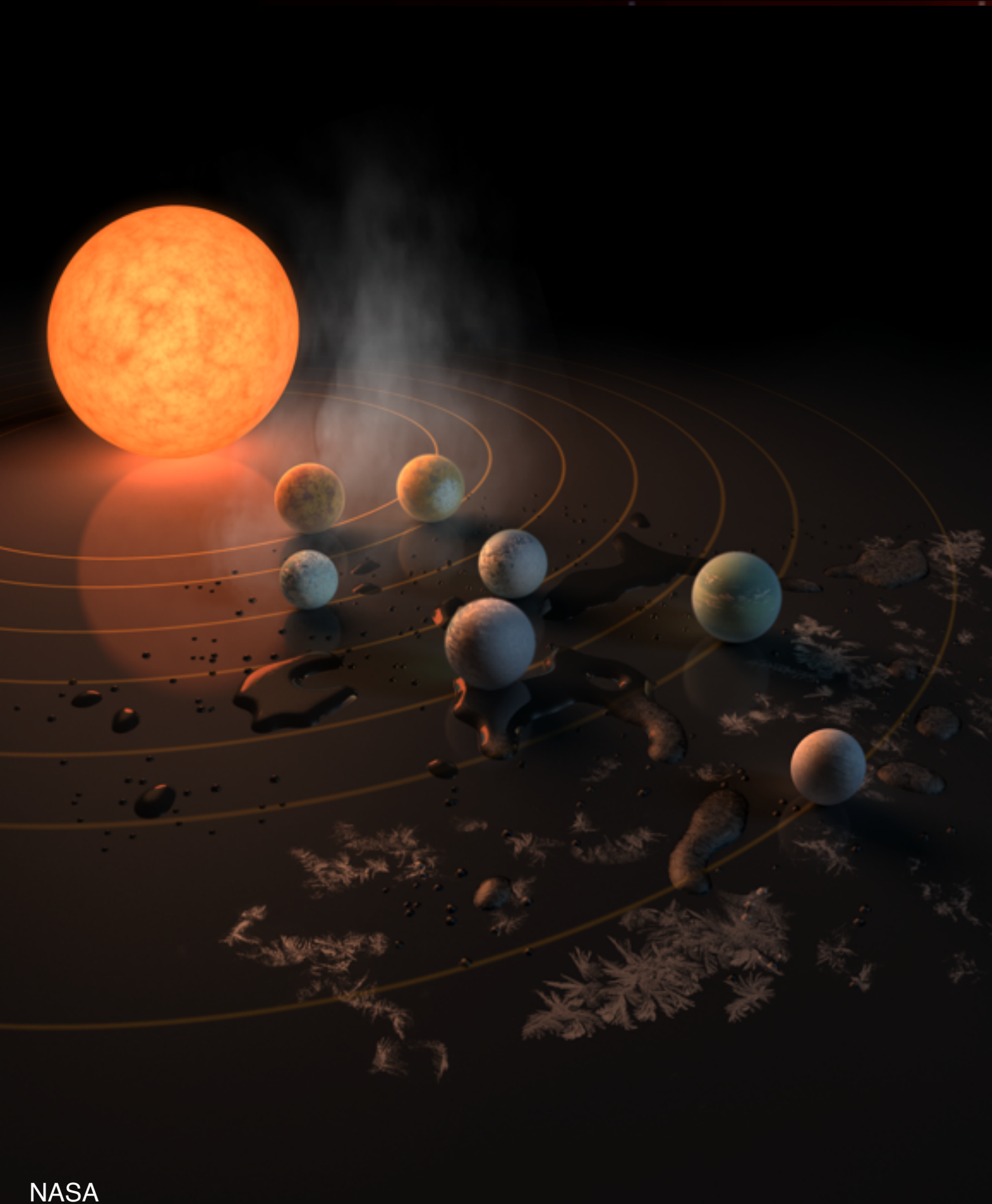
PTF supernova survey: Law et al. 2009



White dwarf transits



Exoplanet habitability & flares





EVR30

The Evryscope (“wide-seer”)

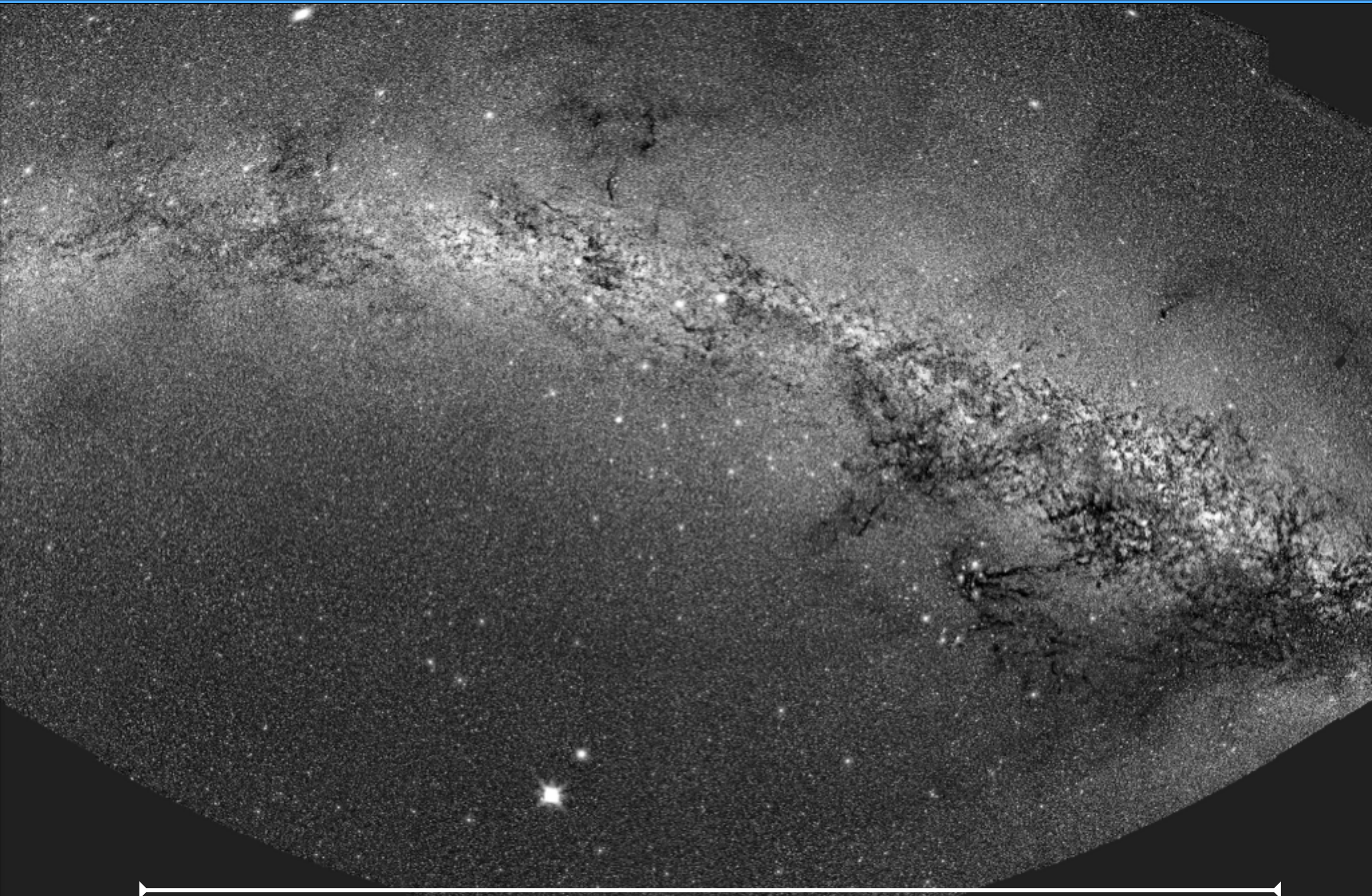


“Bug-eyed” - Popular Mechanics

“Looks more like an architectural folly than a telescope” - Science

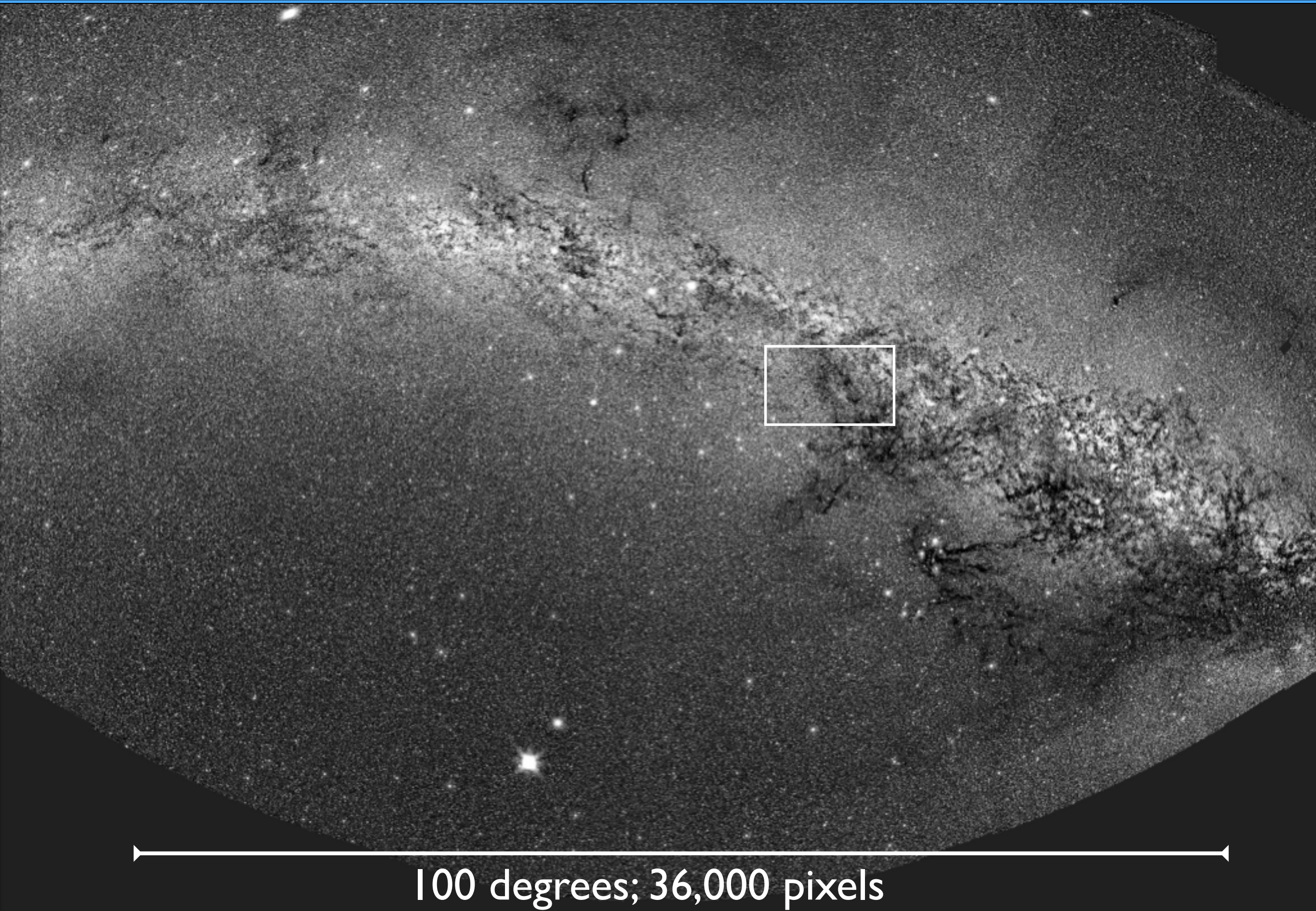
“Like an upside-down colander repurposed into a Star Trek prop”
- Science News

One Evryscope Image

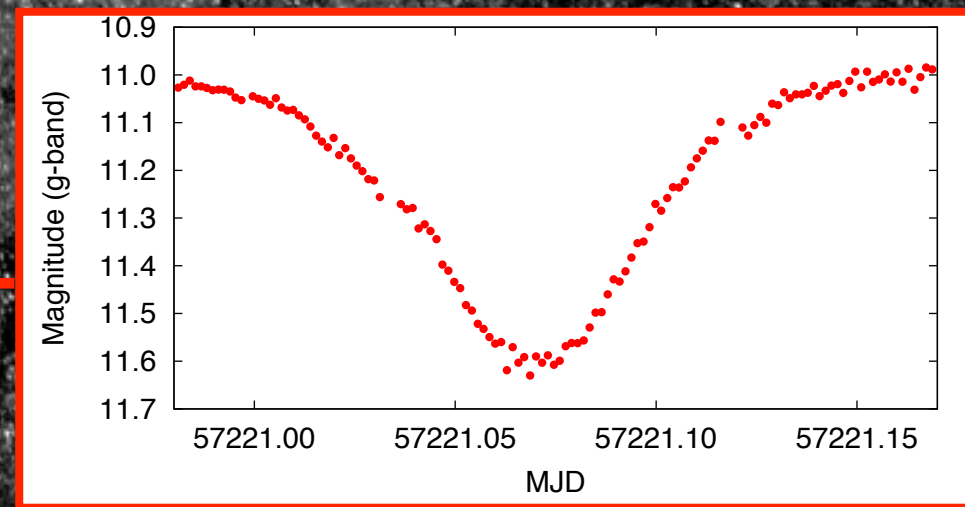
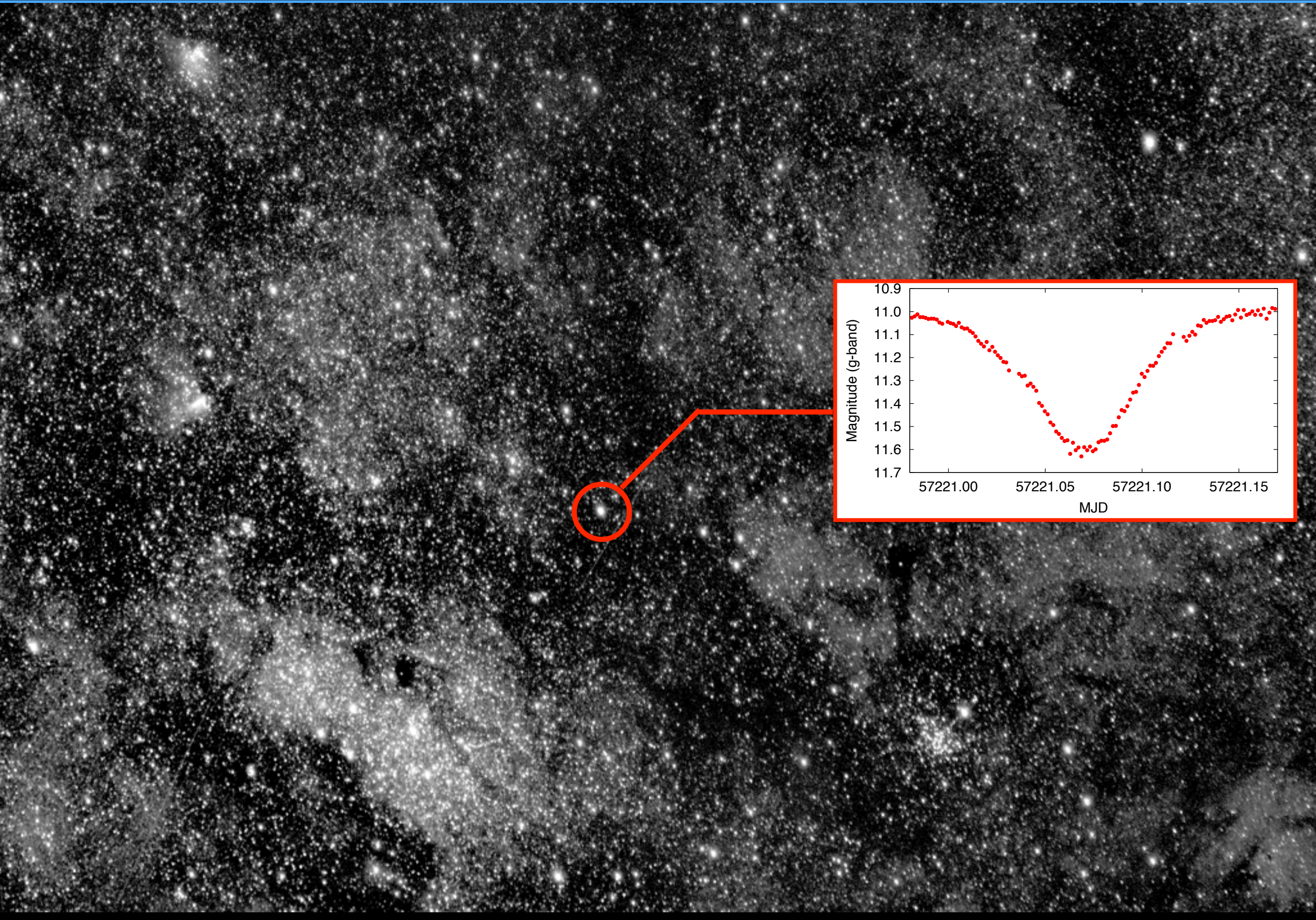


100 degrees; 36,000 pixels

One Evryscope Image



1% of Evryscope field of view



Bright Southern eclipsing binaries

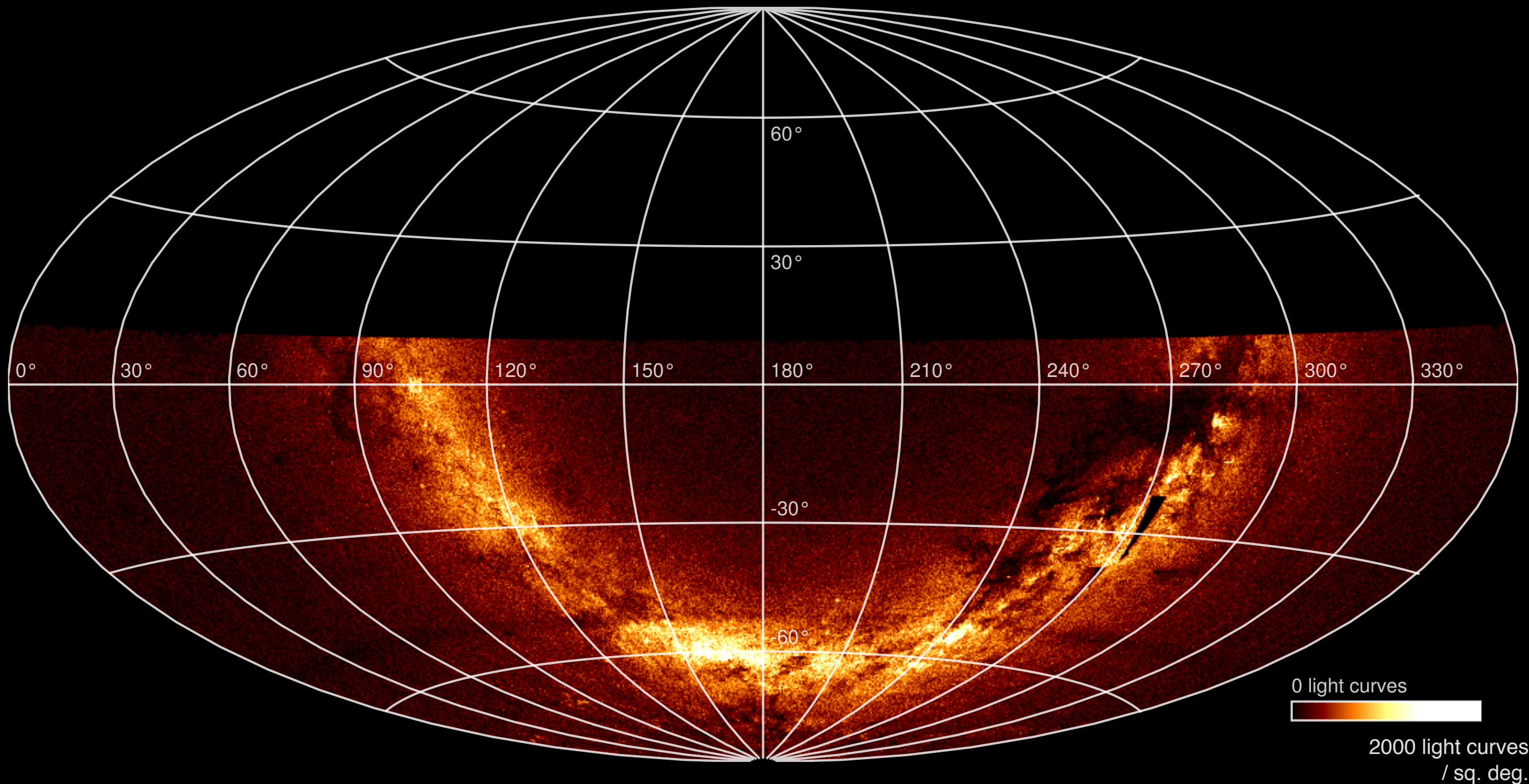


Bright Southern eclipsing binaries



Evryscope DB sky coverage

~1 billion photometric measurements per night
Total imaging data ~1 PB/year.



The Evryscopes



Evryscope-North
MLO, California
Under construction



Evryscope-South
CTIO, Chile

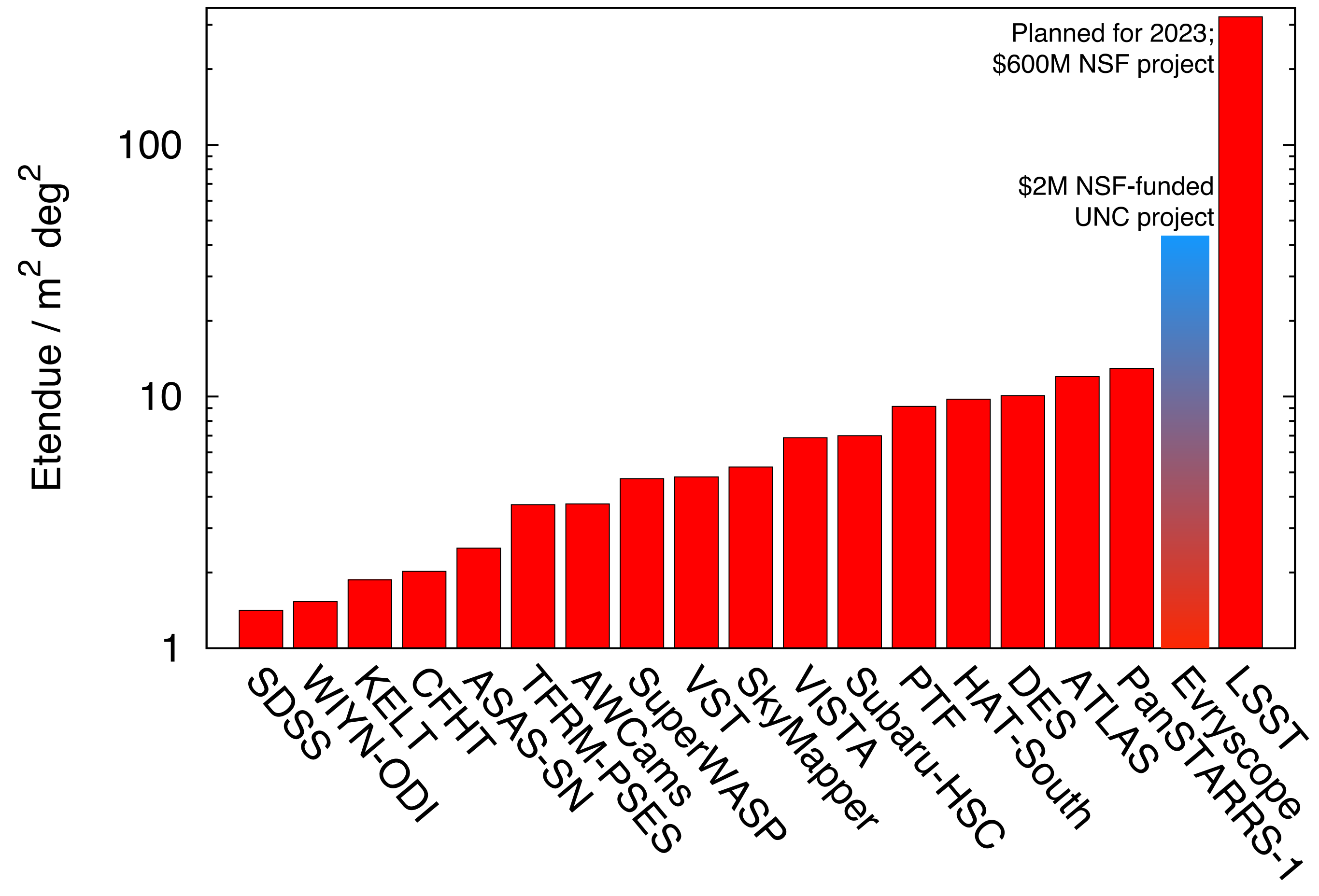
Building Evrscope-North



Building Evryscope-North

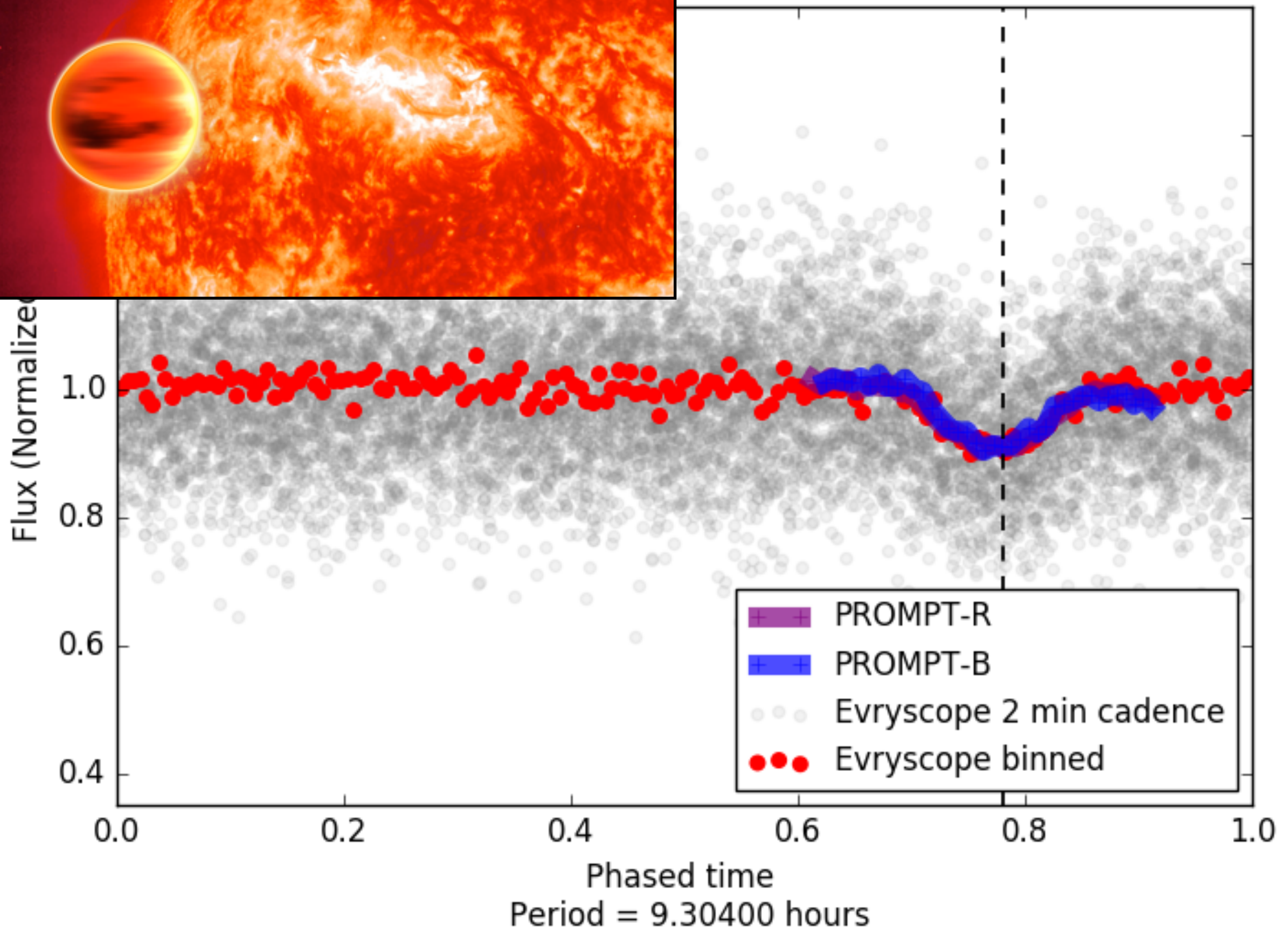
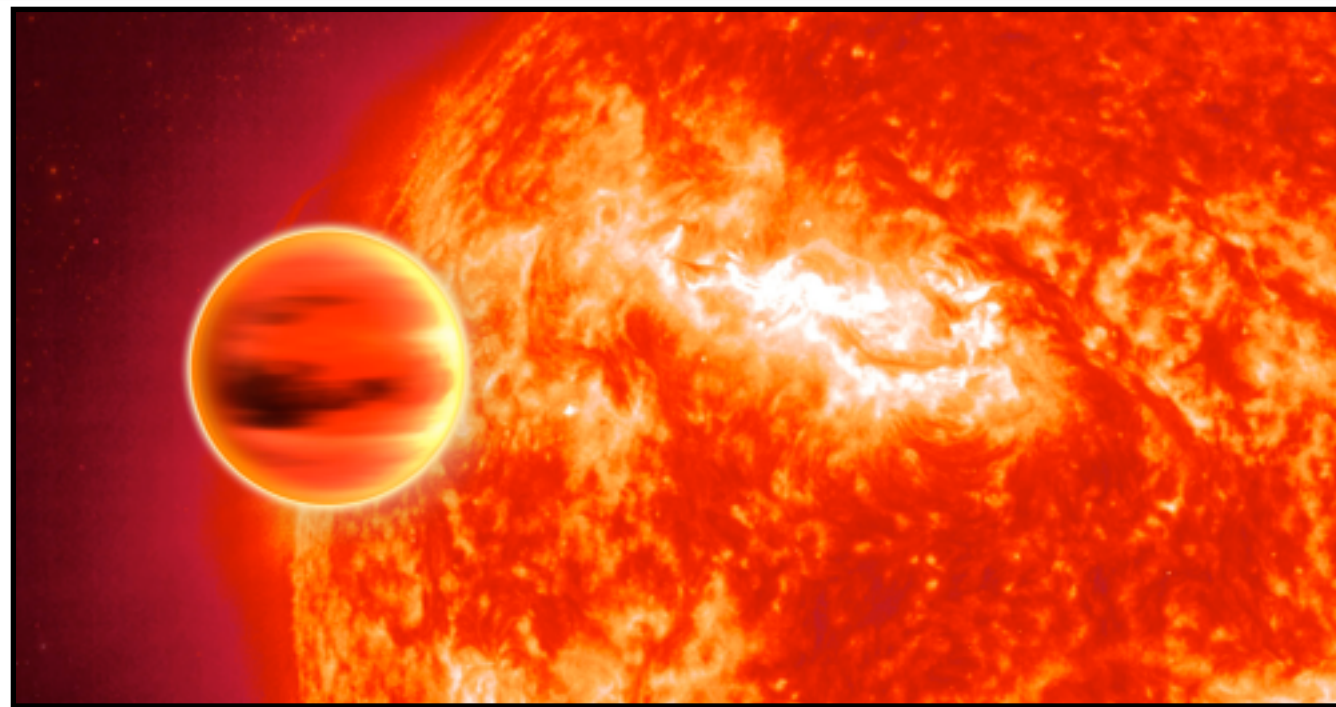


Optimizing sky area instead of telescope size





New planet candidates





PROMPT array
6 1/2m telescopes

11m SALT

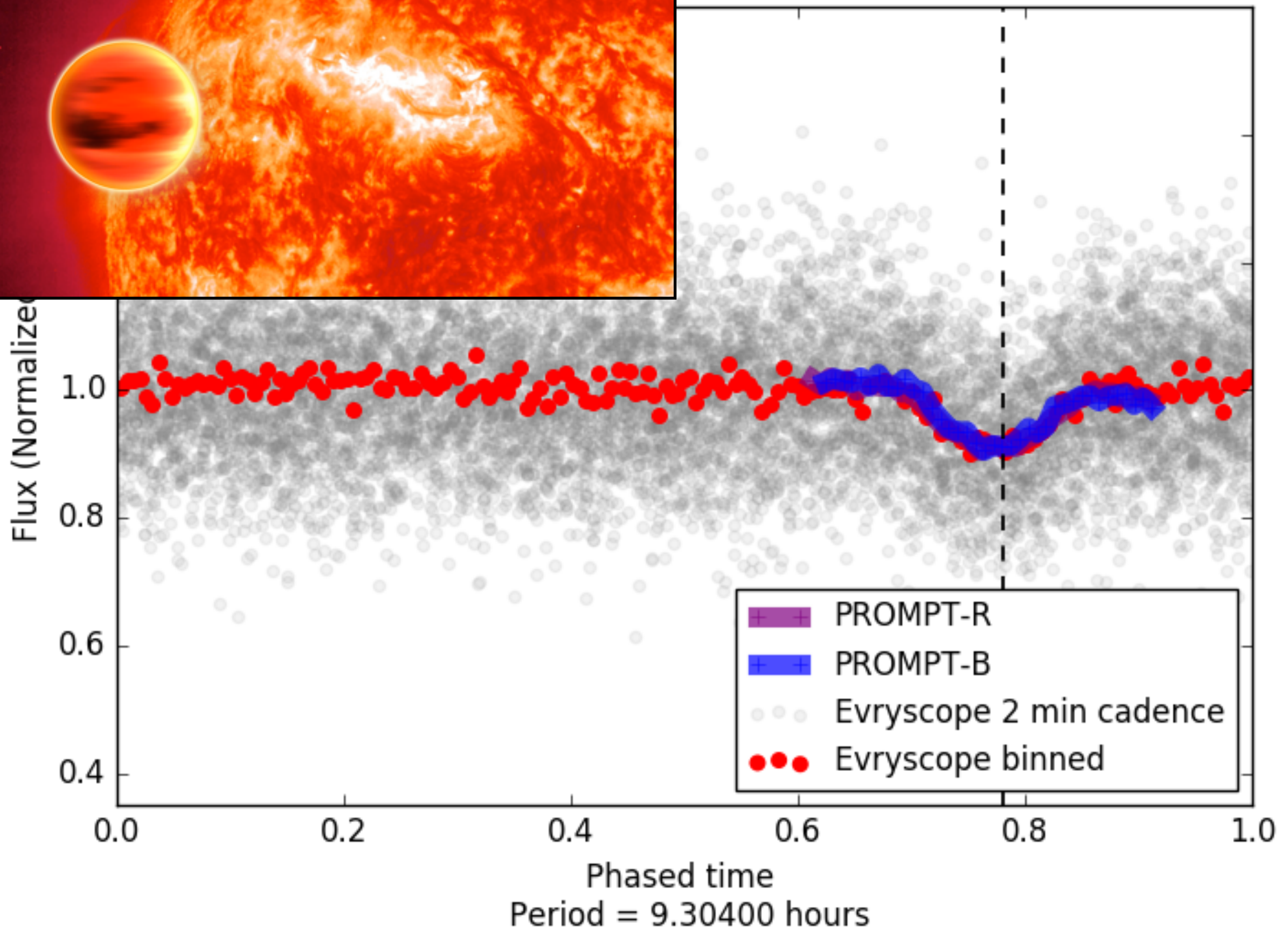
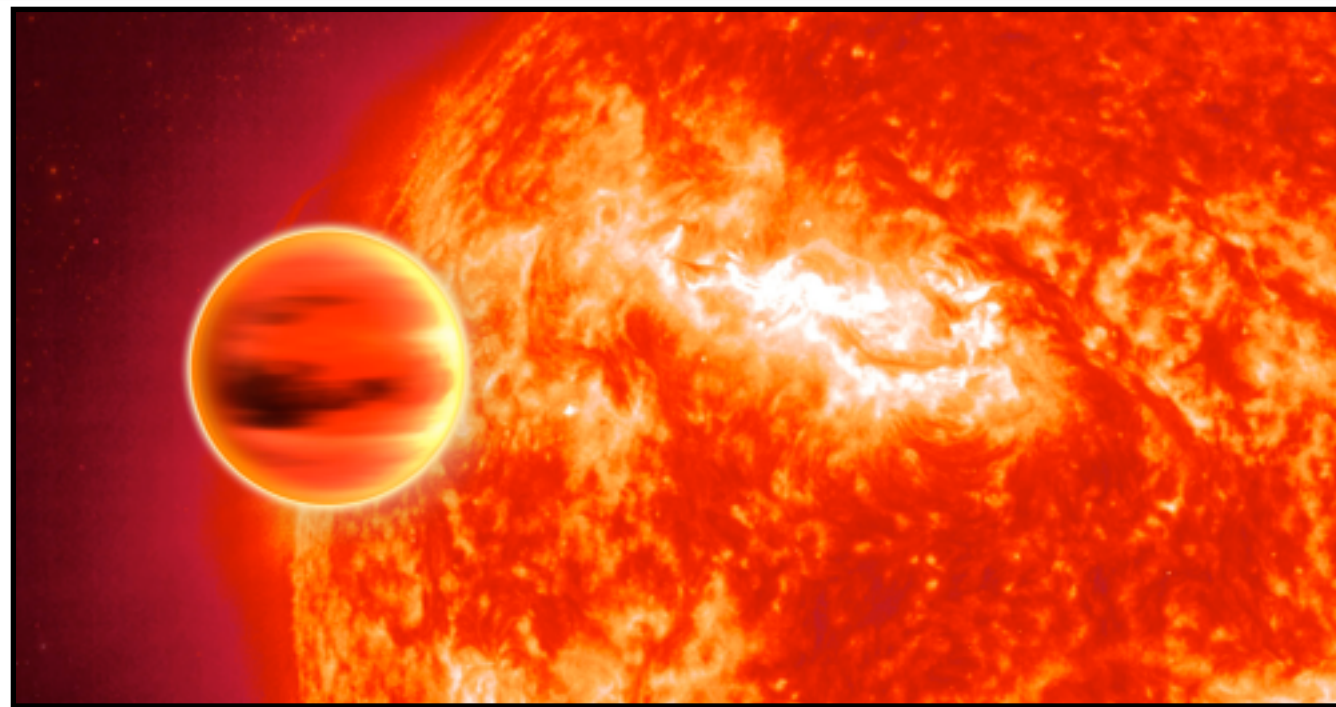
One of the largest optical telescopes in the world

4m SOAR
Spectrographs & high-res imaging

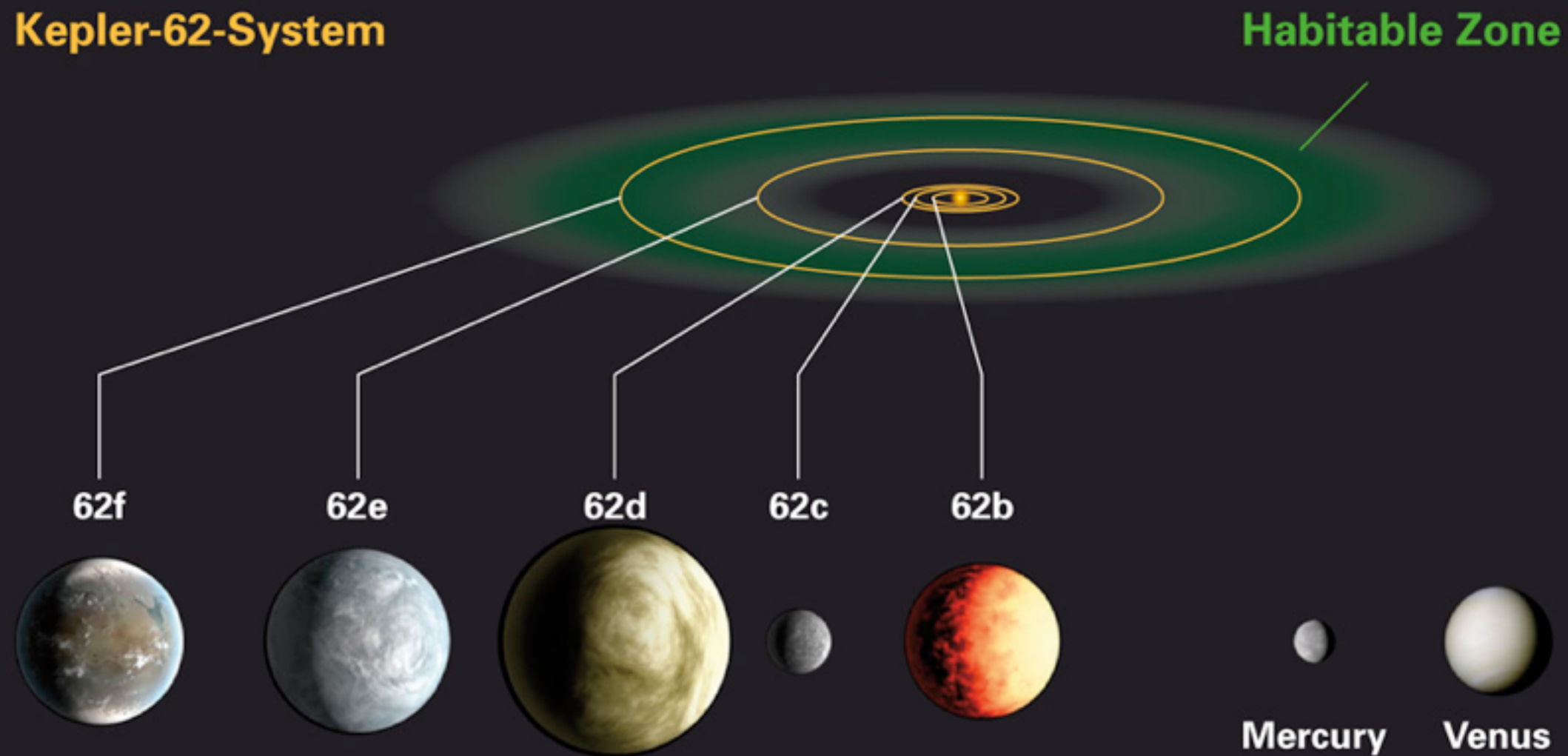
Evryscope:
the first all-sky gigapixel telescope



New planet candidates



Kepler-62-System

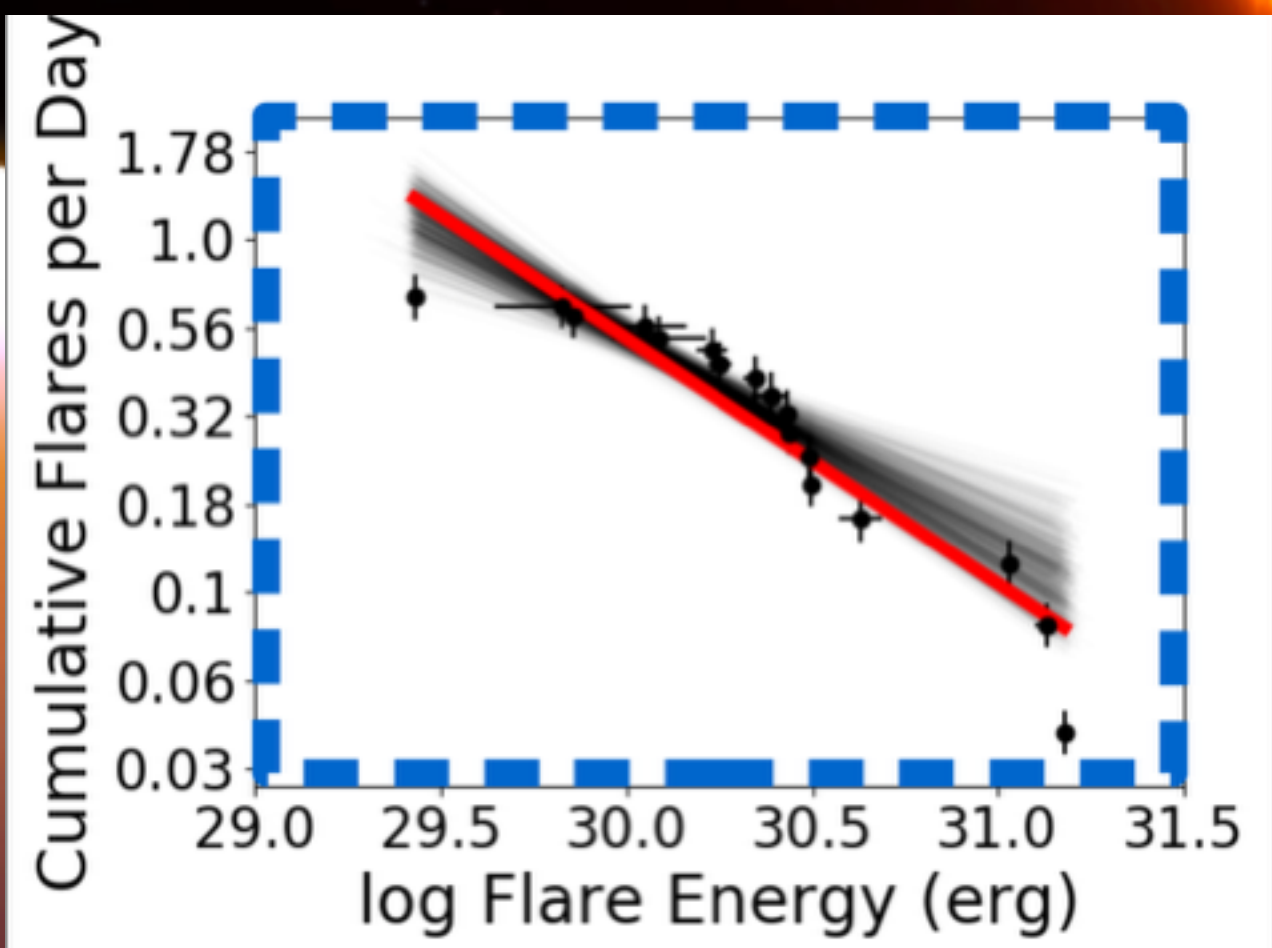
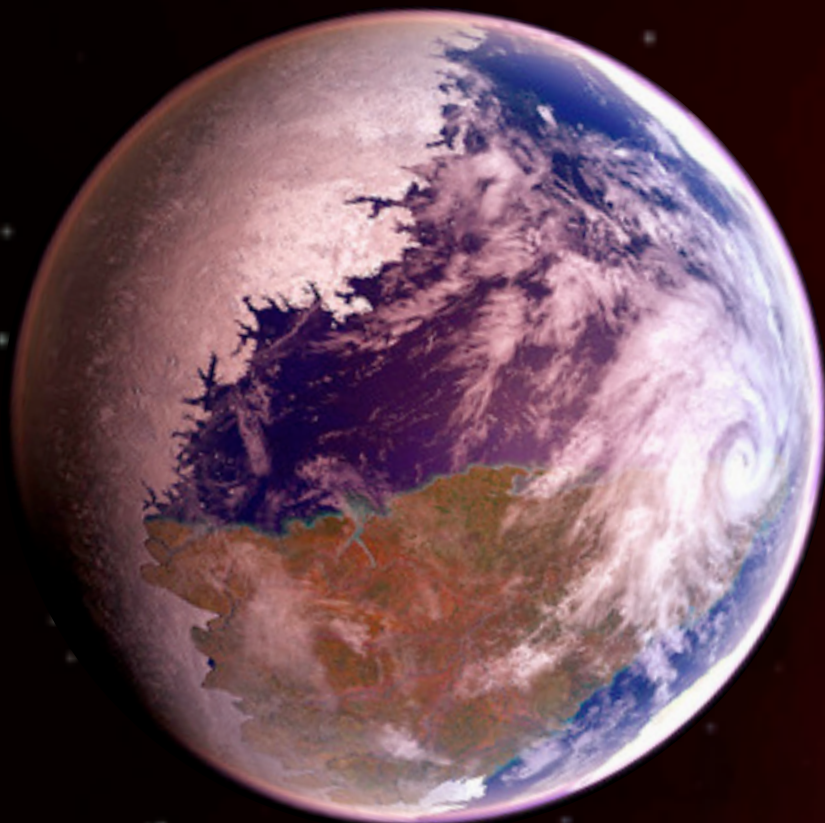


Solar System

Mercury Venus Earth Mars

Habitable Zone





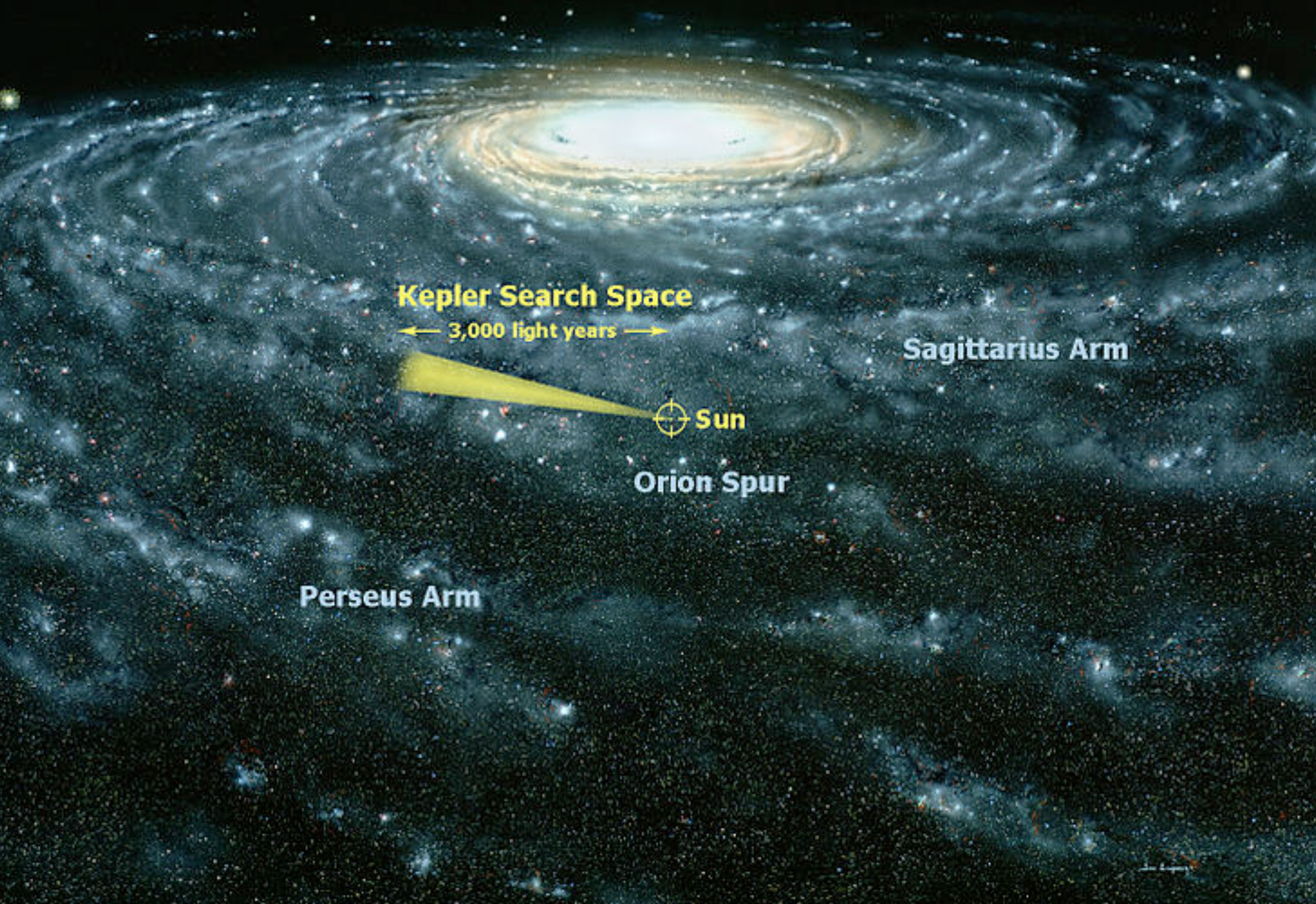
Evryscope results suggest an atmosphere-disrupting superflare every 1-5 years. Ouch.



EVRYS

-
- Spare slides

Milky Way Galaxy



Kepler Search Space

← 3,000 light years →

Sagittarius Arm



Sun

Orion Spur

Perseus Arm

20% of Sun-like stars have Earth-sized planets in the habitable zone
>50% of cool stars have potentially habitable worlds

Kepler Search Space

← 3,000 light years →

Sagittarius Arm

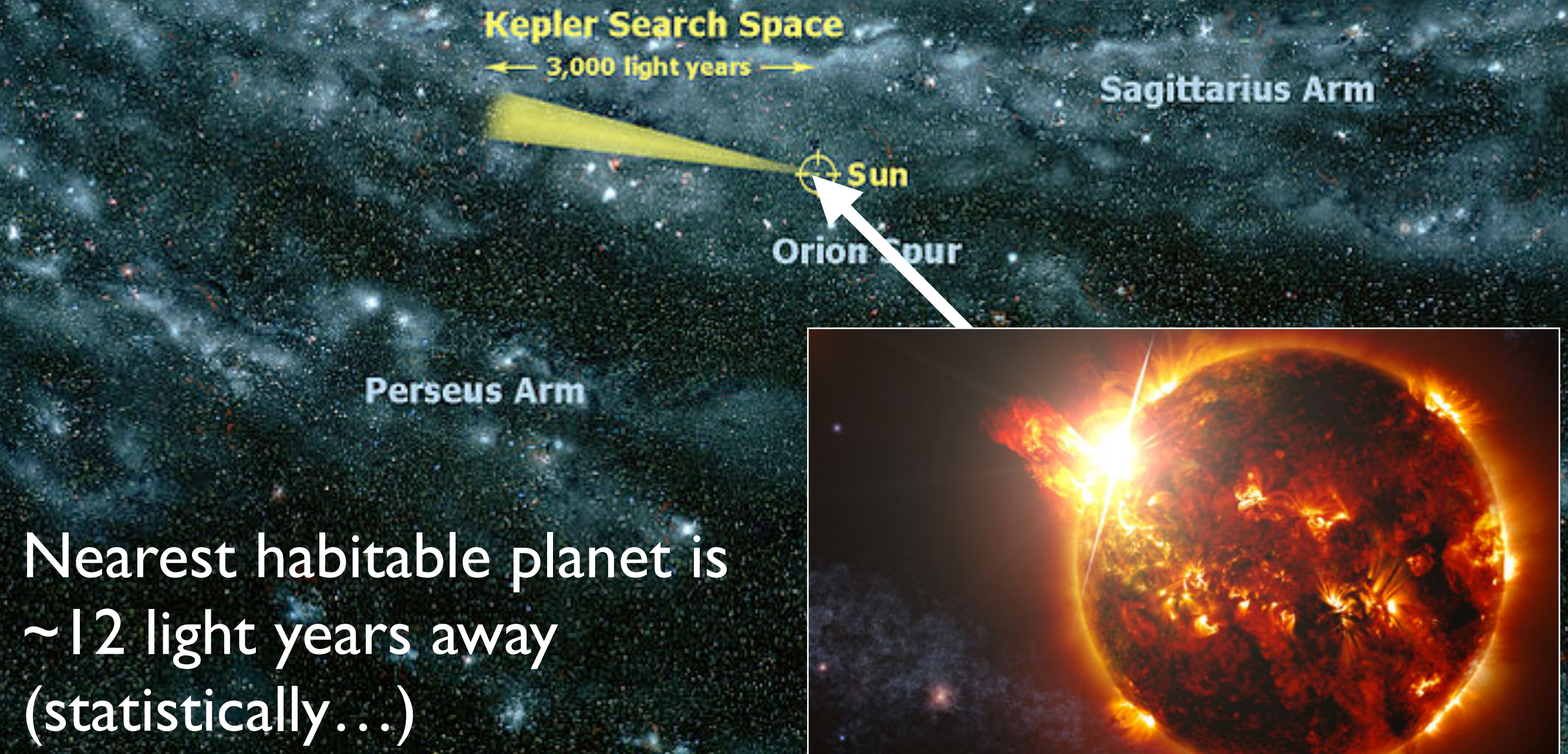
Sun

Orion Spur

Perseus Arm

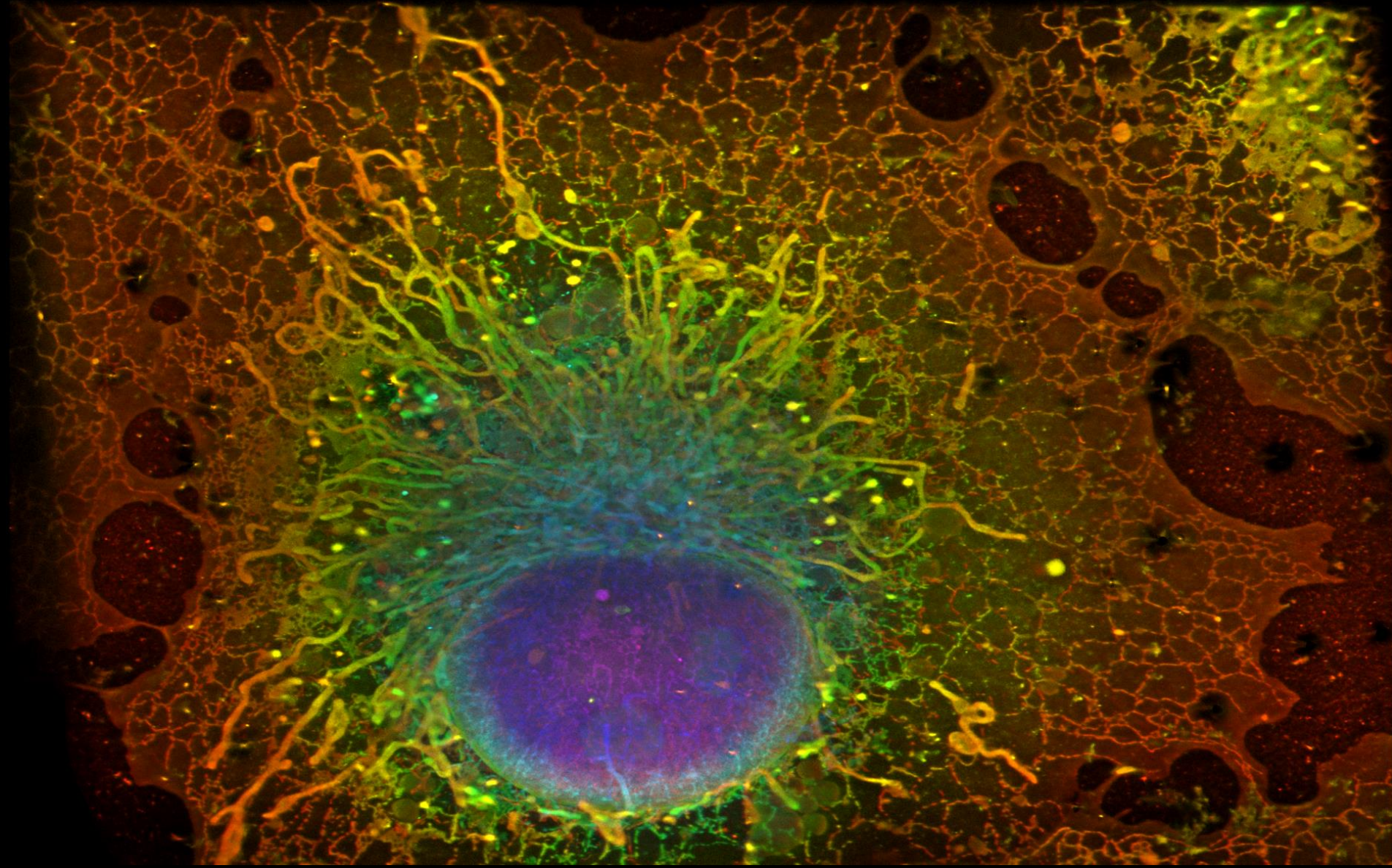
Nearest habitable planet is
~12 light years away
(statistically...)

20% of Sun-like stars have Earth-sized planets in the habitable zone
>50% of cool stars have potentially habitable worlds



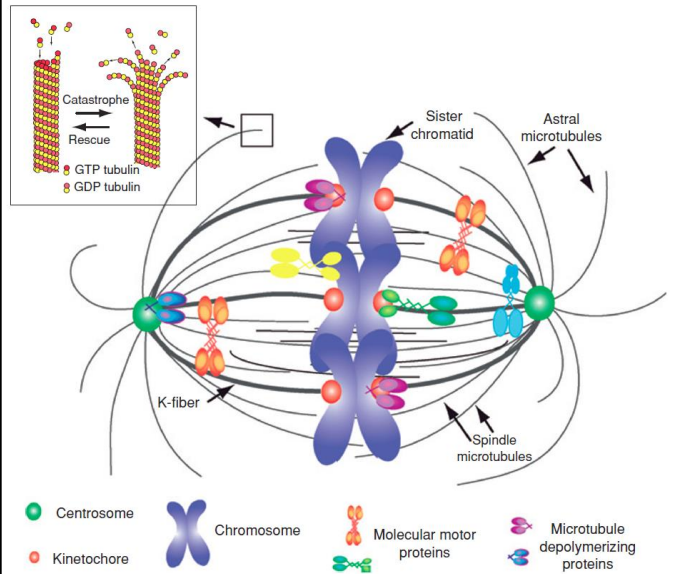
Nearest habitable planet is
~12 light years away
(statistically...)

From molecules to organisms: pushing the limits of fluorescence microscopy



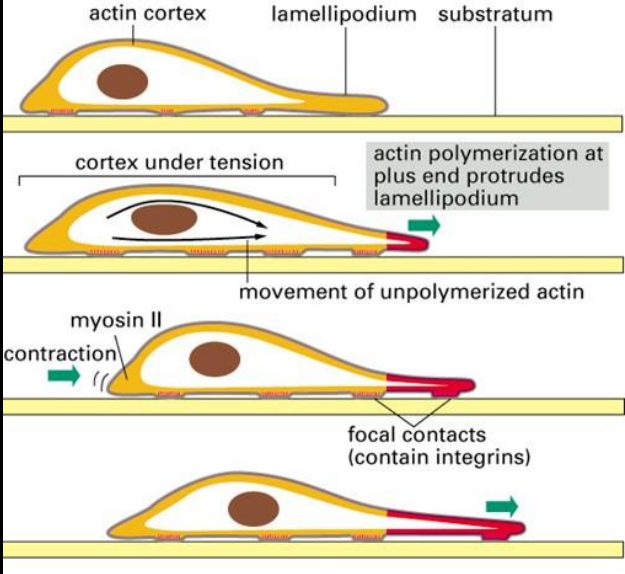
Wesley R. Legant
Departments of Pharmacology and BME
University of North Carolina, Chapel Hill

Animated Cell Biology – From Diagrams to Movies



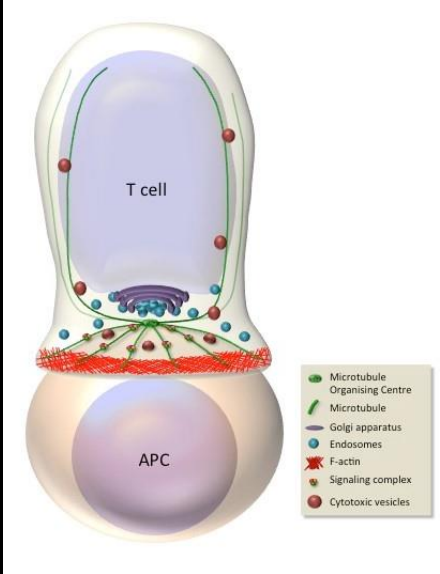
Walczak C.E.. et al., *Int Rev Cytology* 2008

Cell Division



Molecular Biology of the Cell 2002

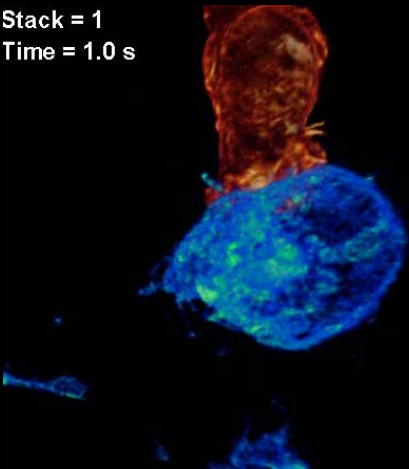
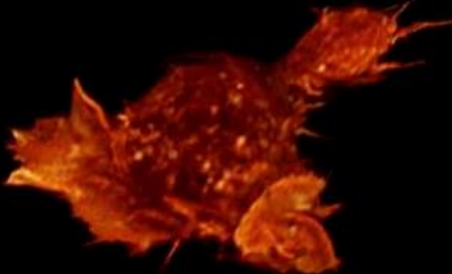
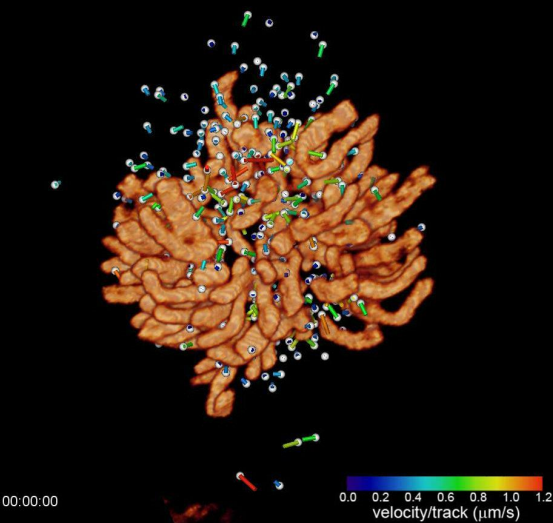
Cell Migration



Alcover et al. 2018

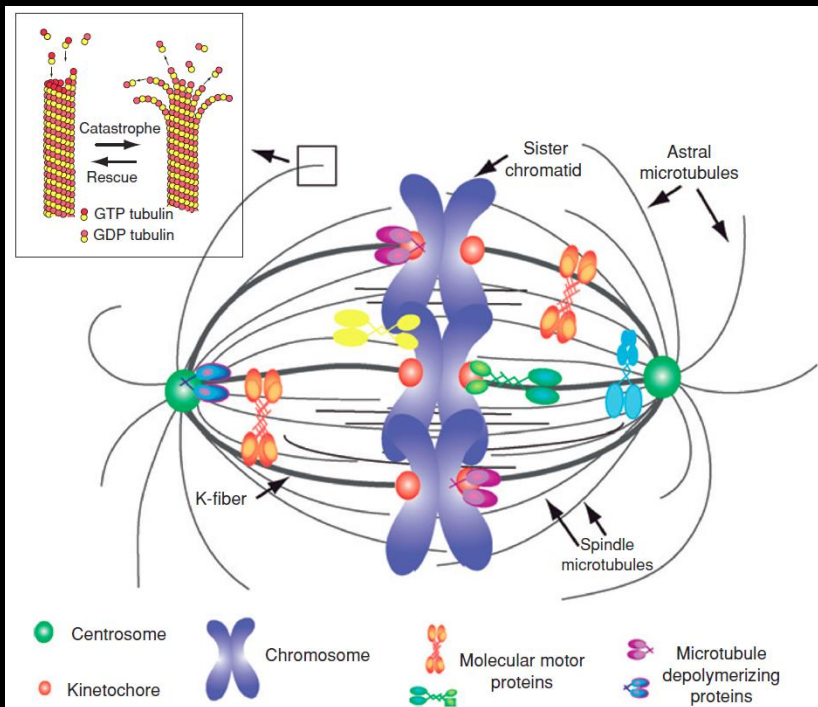
Immune Function

prometaphase HeLa cell tracked GFP-EB1 tagRFP - H2B

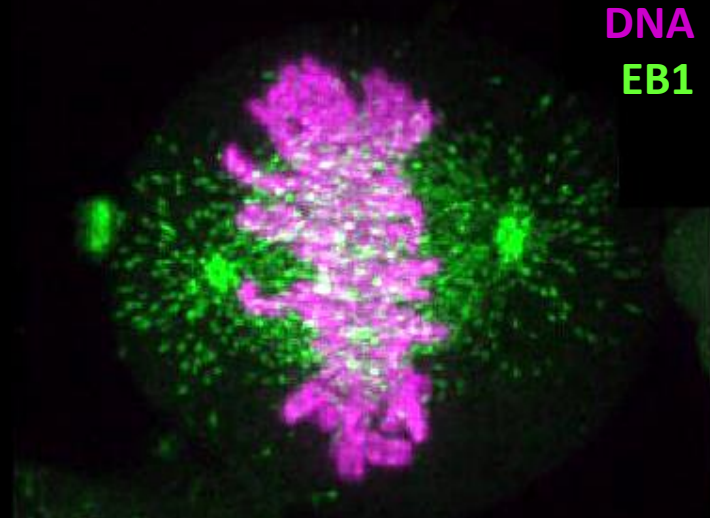


Imaging Cell Division

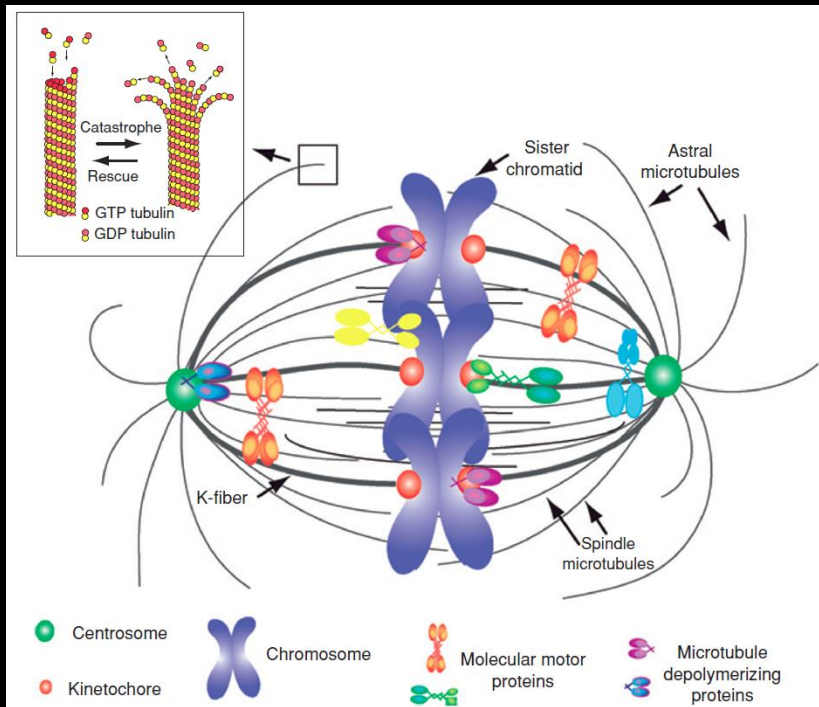
normal



Walczak C.E., et al., *Int Rev Cytology* 2008

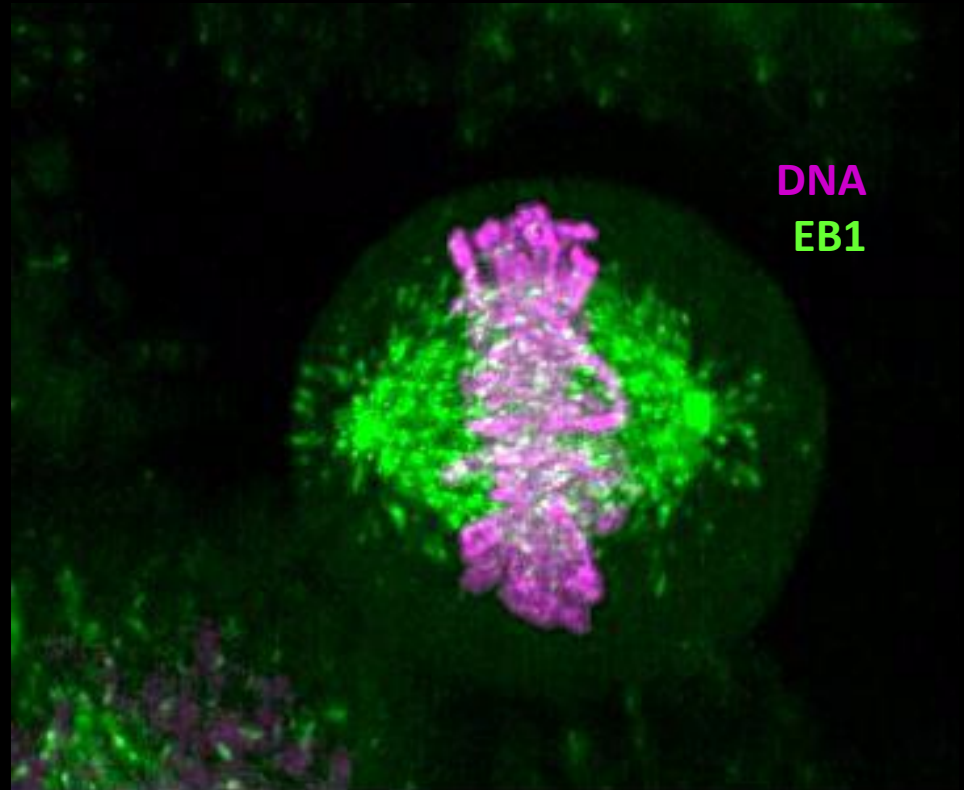


Imaging Cell Division



Walczak C.E., et al., *Int Rev Cytology* 2008

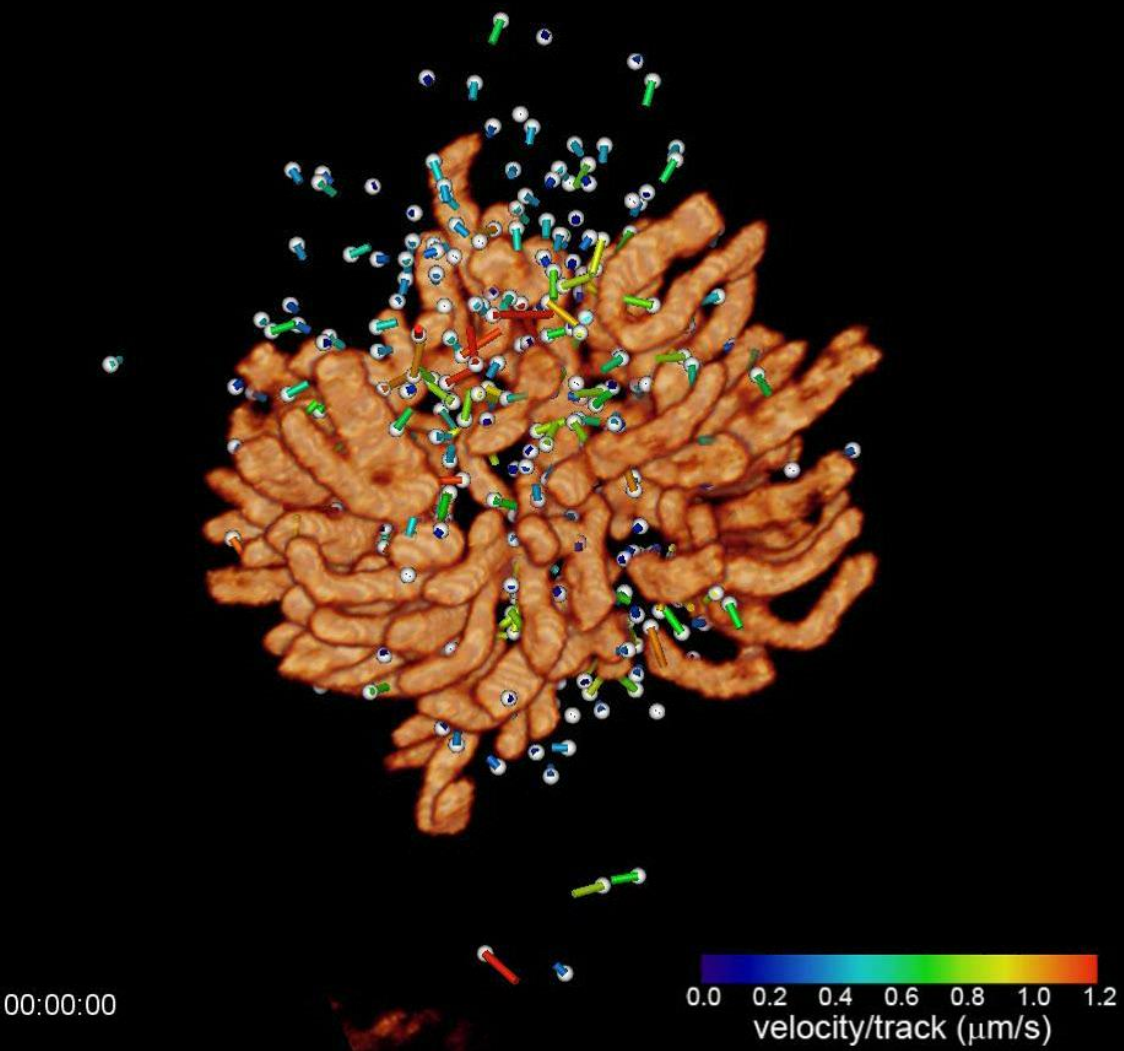
abnormal



Imaging Cell Division

prometaphase

HeLa cell tracked GFP-EB1 tagRFP - H2B



Technology

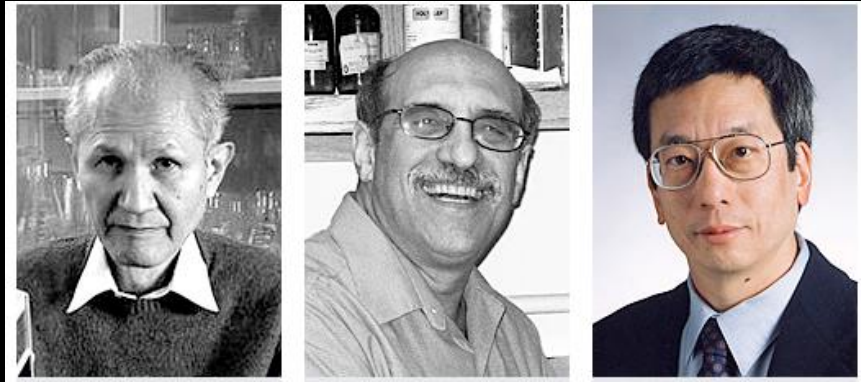
Applications

Collaborations

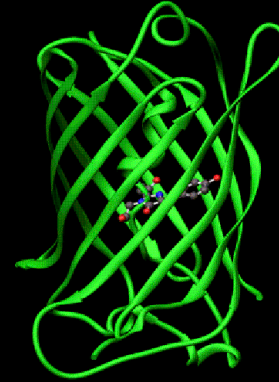
Future

Protein Specific Live Cell Fluorescence Imaging

Shimomura, Chalfie, & Tsien



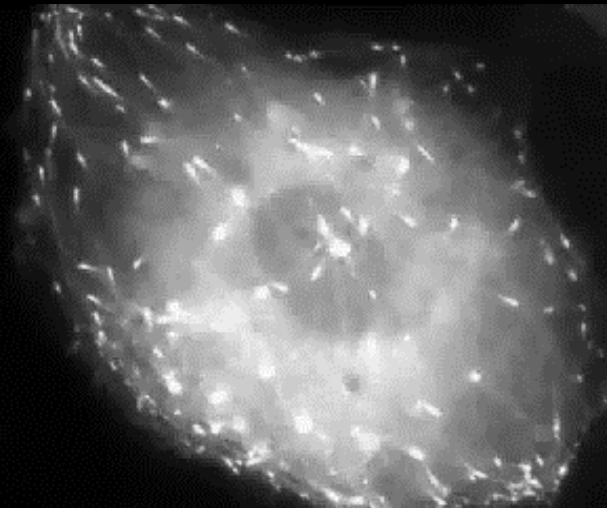
1994: green
fluorescent protein



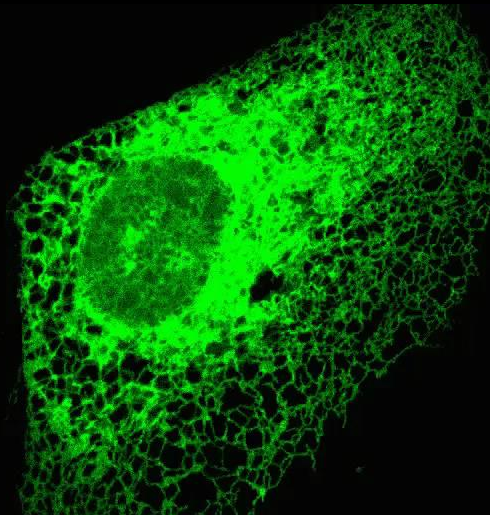
2008: Chemistry Nobel



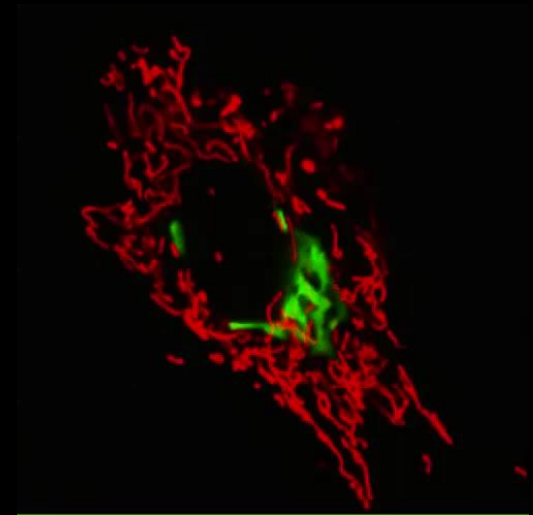
microtubule ends



endoplasmic reticulum



golgi, mitochondria

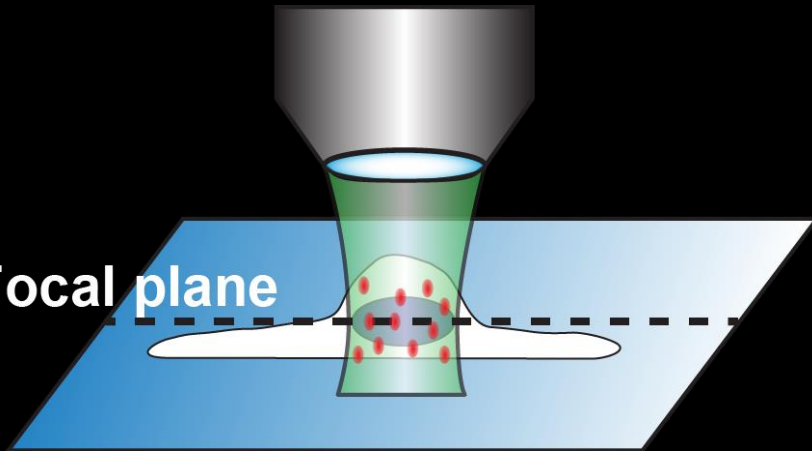


Technology truly enabled by the Nobel Prizes of 2008 and 2009 (GFP and CCDs)

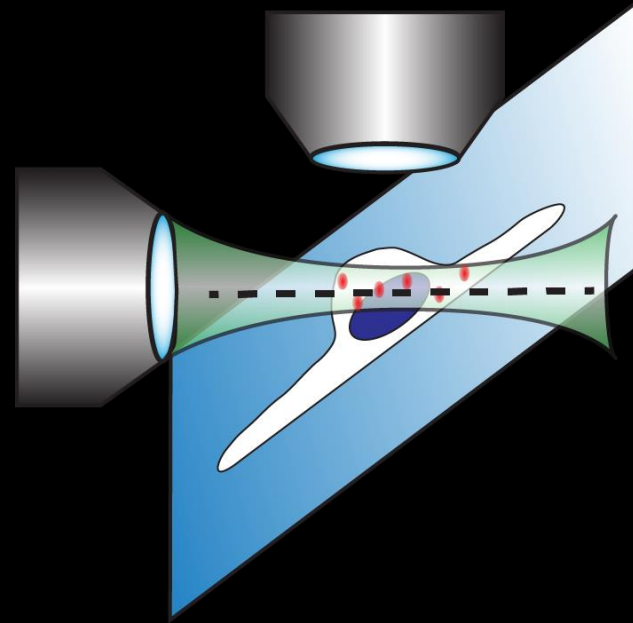
Challenge - Phototoxicity, Background, Speed

Widefield

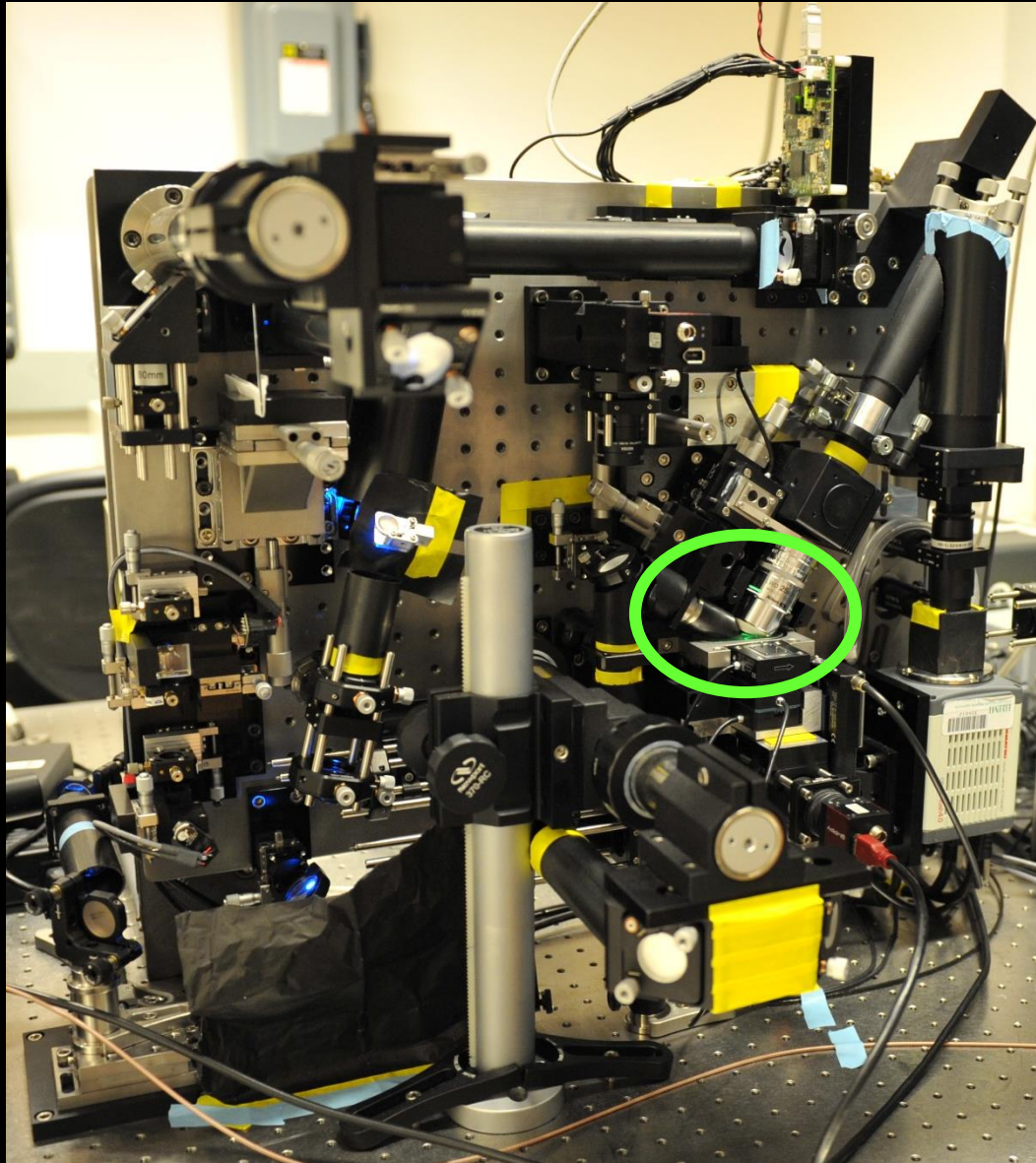
Focal plane



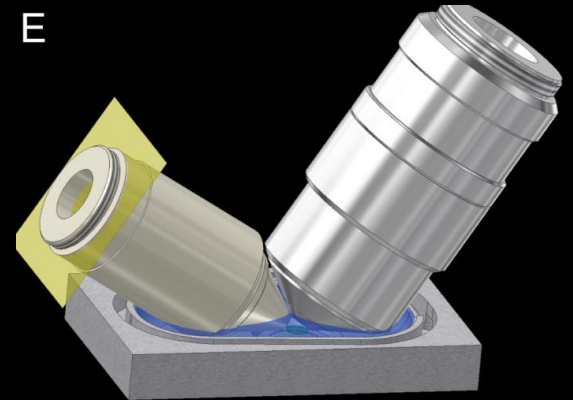
Lightsheet



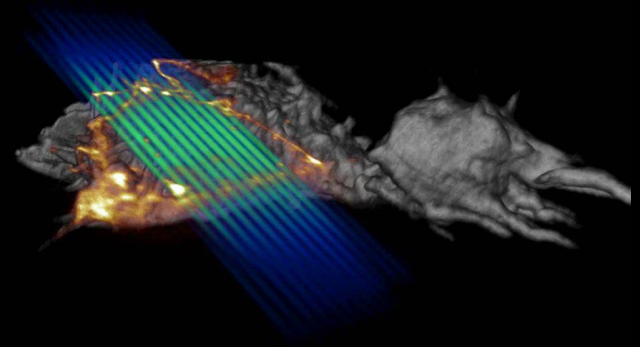
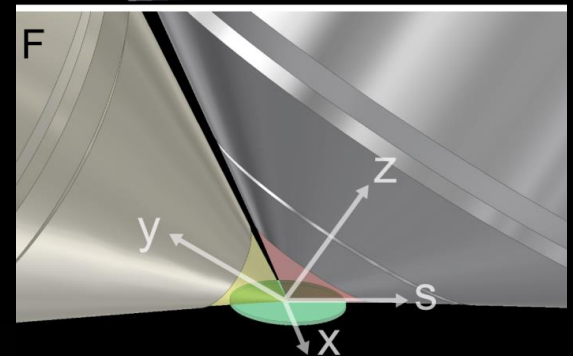
Lattice Light Sheet Microscopy



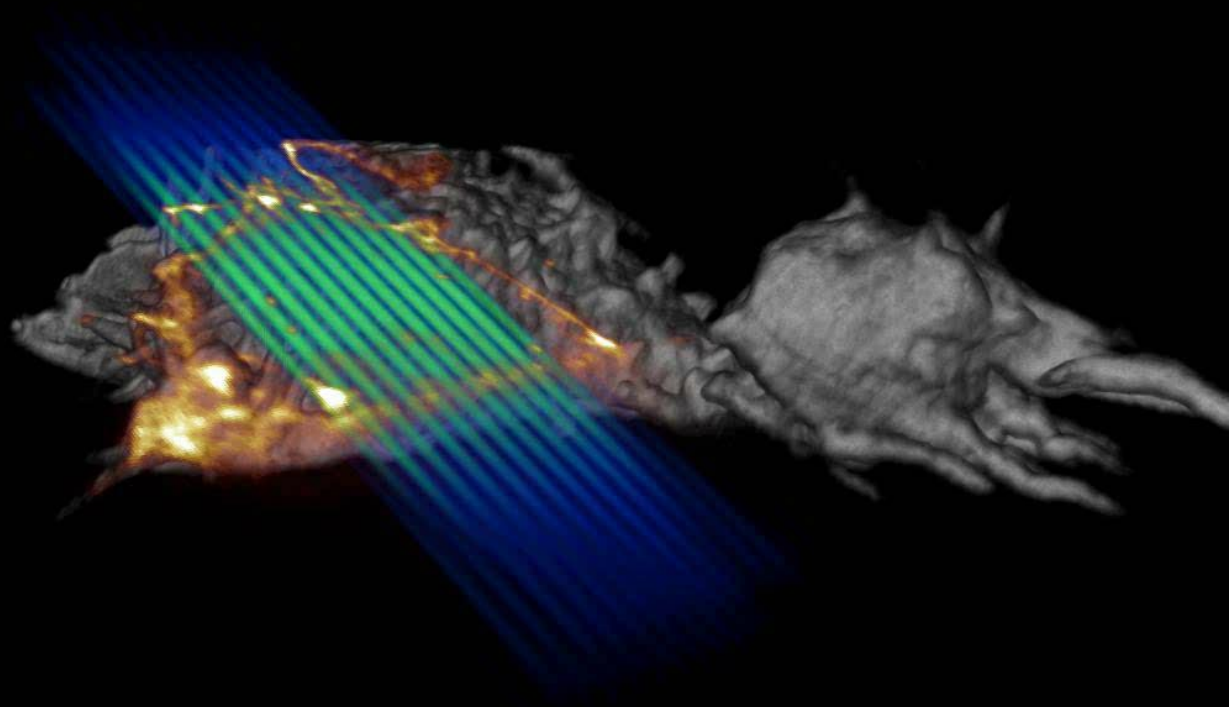
E



F



Chen BC.*, Legant W.R.*, Wang K.* *et al.*, *Science* 2014

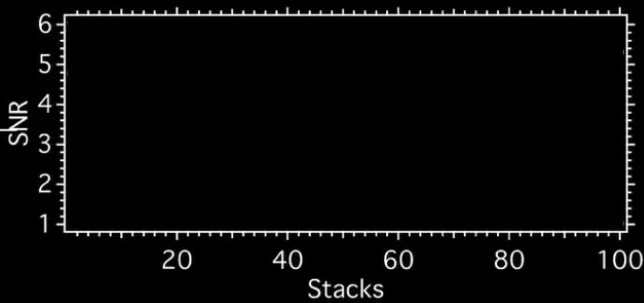


Lattice Light Sheet vs. Commercial Spinning Disc

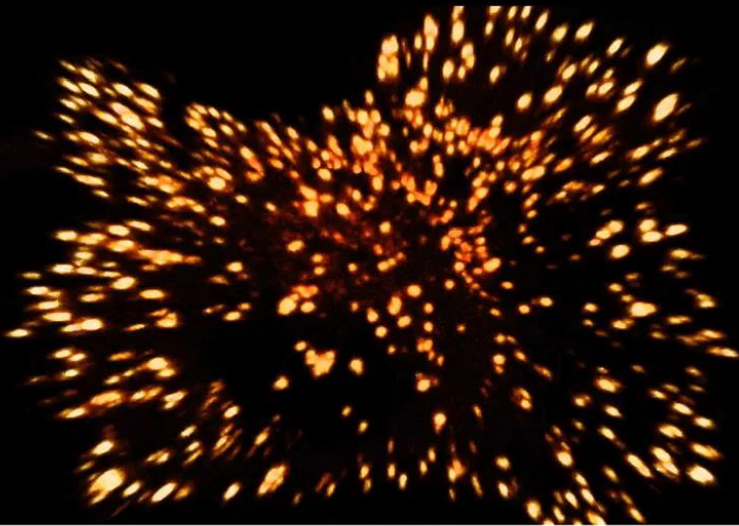
Spinning Disk

0.3µm z-sampling
50 z-planes /stack
~6 sec interval / stack

Cells gene-edited to express
AP2-eGFP



Stack#
0
~107nm/px
10 µm



Stack#
0
~104nm/px
10 µm



LLSM

0.3µm z-sampling
Gene-edited AP2-eGFP
100 optical sections /stack
~6 sec interval / stack



Summary

Lattice light sheet microscopy

(Chen BC*, Legant WR*, Wang K* et al. *Science*, 2014)

- reduced background fluorescence
 - less photodamage
-
- Full documentation, parts lists, software via RLA through HHMI
 - >80 licensees, 5 continents, >30 clone instruments
 - 3 patents, commercially licensed

HHMI Janelia Research Campus



Eric Betzig



Kai Wang



Bi-Chang Chen



Wesley Legant

Technology

Applications

Collaborations

Future

How do cells migrate through three-dimensional space?

- development, wound healing

HL-60 cell

mCherry - utrophin FITC - collagen

- cancer metastasis

- immune function

- Biochemistry

 - parts list

 - interactions

 - functions

3D Cellular Gait Analysis

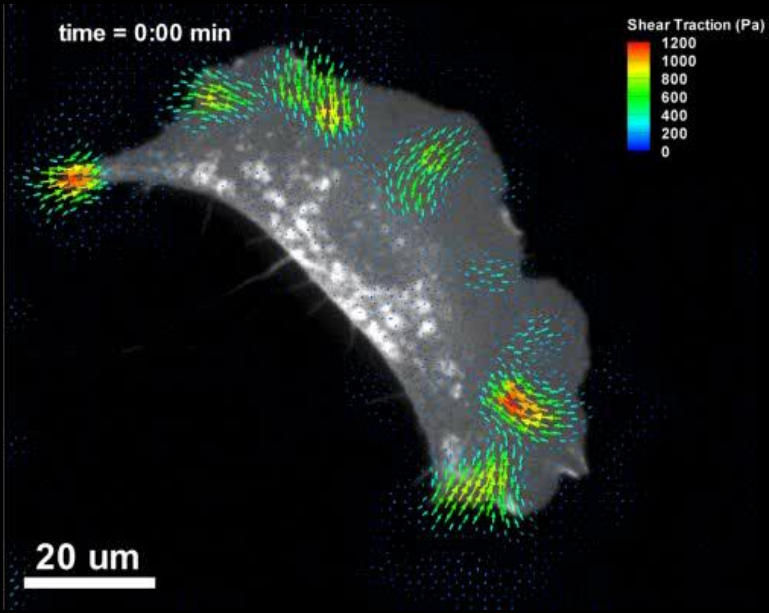
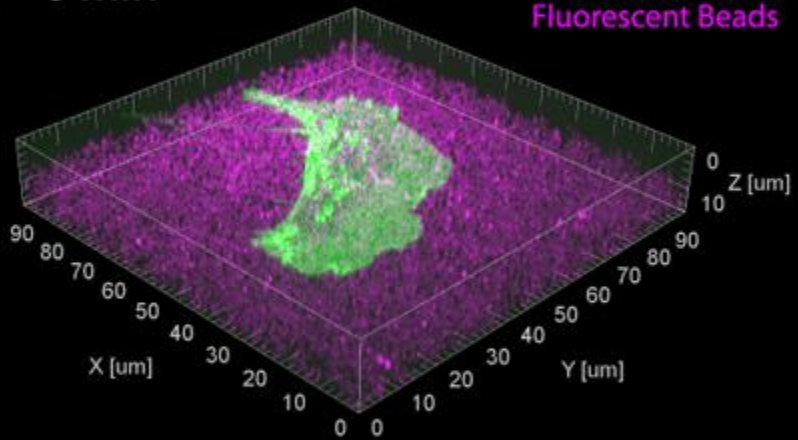
Current Models of Cell Migration

2D imaging of cells in culture



t = 0 min

mEGFP-Farnesyl
Fluorescent Beads



conventional microscopes

Quantitative Measurements of the 3D Cellular Gait

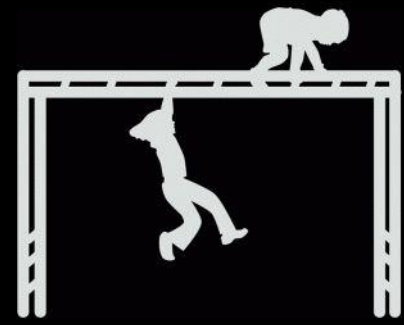
3D imaging of cells on glass



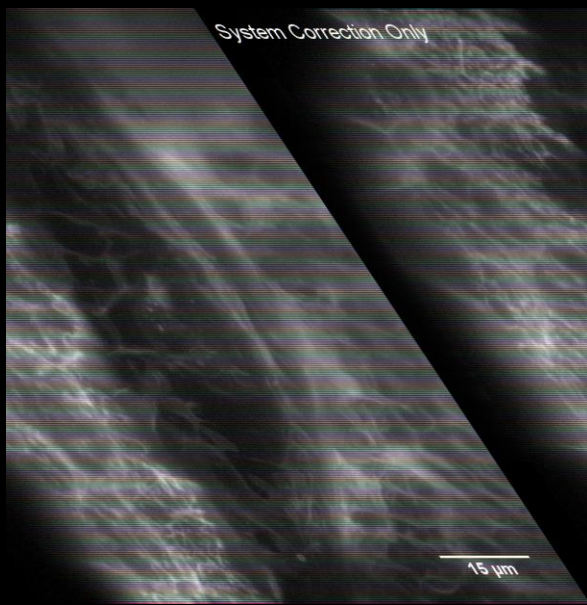
3D imaging of cells in model matrices



3D imaging of cells in vivo



HL-60 cell
mCherry - utrophin FITC - collagen



lattice light sheet

lattice light sheet +
3D cell culture

lattice light sheet +
adaptive optics

Liu TL. et al. submitted 2018

Technology

Applications

Collaborations

Future

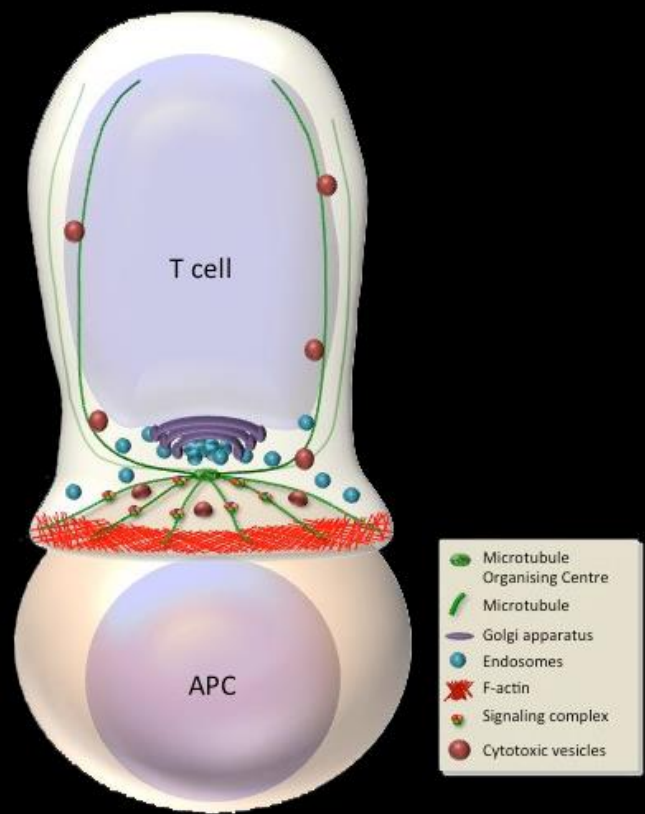
How do immune cells target diseased/infected cells in the body?

- Infectious disease
- cancer immunotherapy
 - 714 active/recruiting/pending clinical trials for cancer immunotherapy in the USA¹
 - 35 clinical trials currently at UNC
 - 10 year timeline is estimated \$30-75 billion in sales²
 - Not all patients respond and it's often unknown why

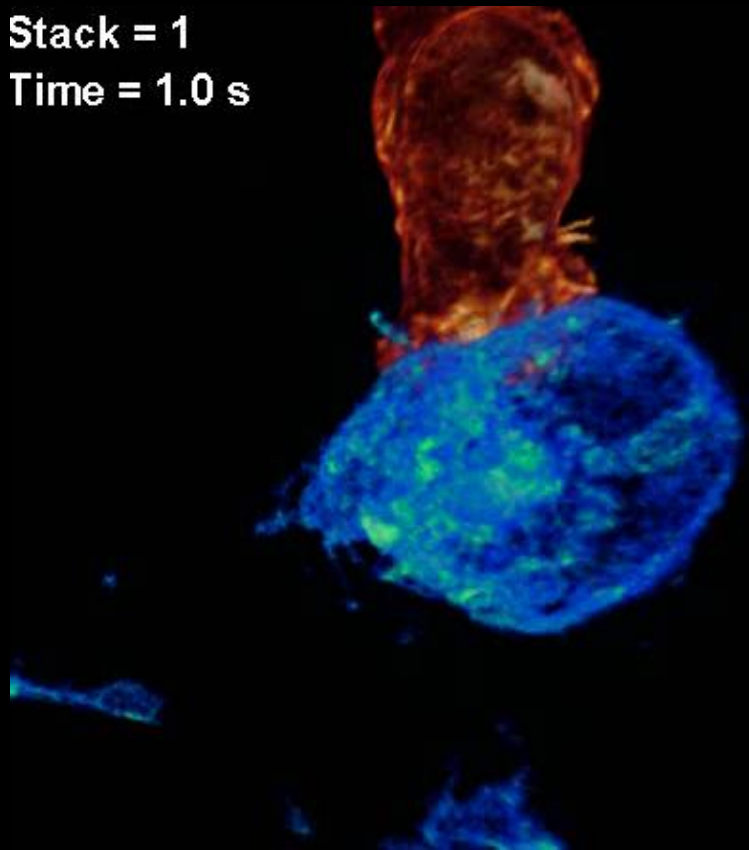
How does the specialized structure between a T-cell and target cell form?

- 1) clinicaltrials.gov
- 2) Park A., "What if your immune system could be taught to kill cancer?" Time Magazine, 3/24/2016

Imaging the Immune Synapse



Stack = 1
Time = 1.0 s



<https://research.pasteur.fr/en/project/intracellular-vesicle-traffic-drives-immunological-synapse-formation-and-t-cell-activation-inhibition-by-human-immunodeficiency-virus-hiv-1/>

Chen BC.*, Legant W.R.*, Wang K.* *et al.*, *Science* 2014

HHMI Janelia



Wesley Legant

NIH/HHMI Janelia



Alex Ritter

University of Cambridge



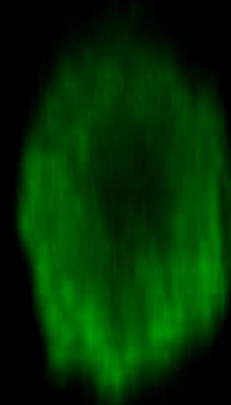
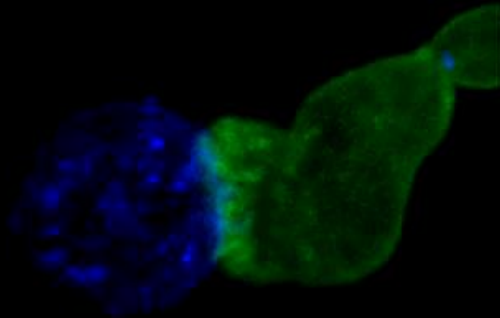
Jennifer Lippincott-Schwartz



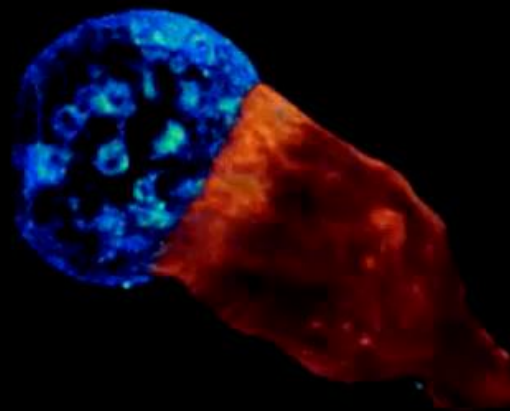
Gillian Griffiths

Imaging the Immune Synapse

Commercial
Spinning Disc
Confocal



Lattice Light
Sheet

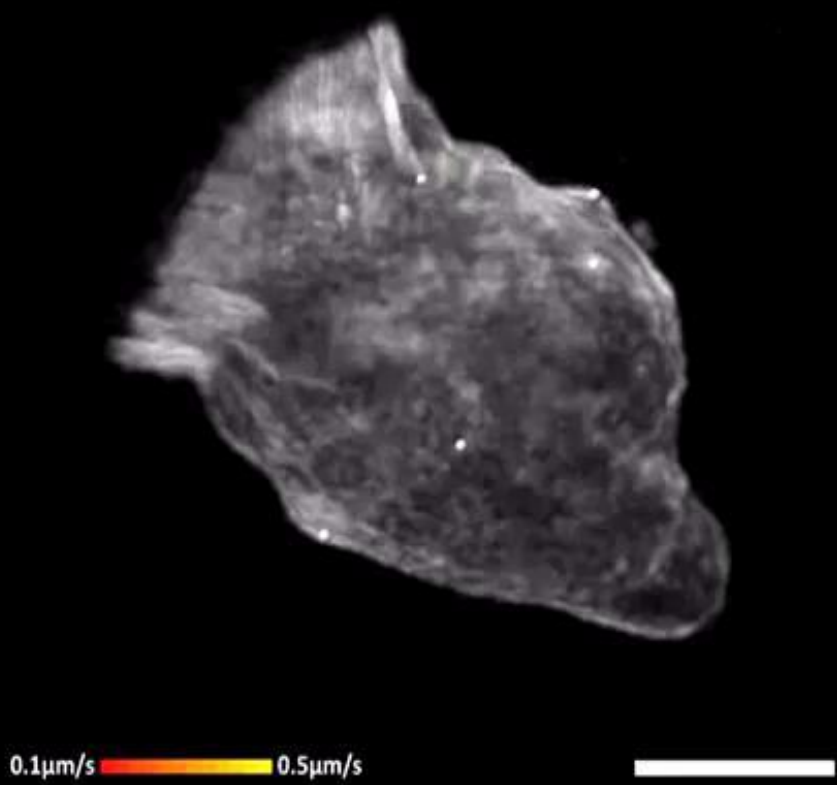
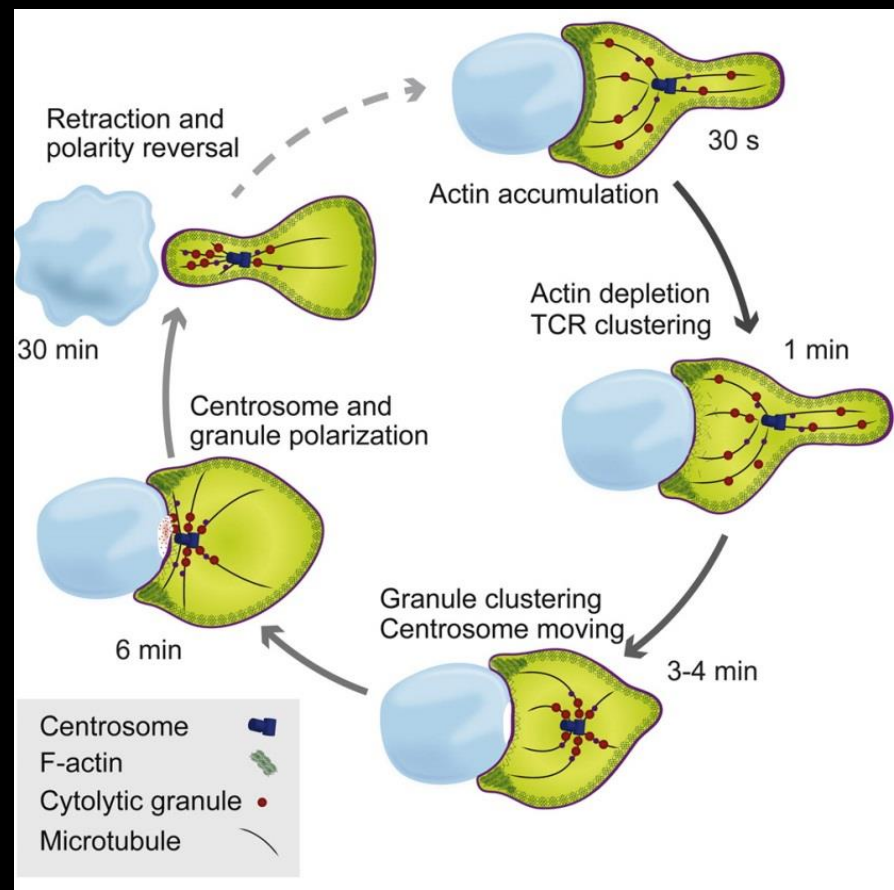


S2C



Stack = 0
Time = 0.0 s

Imaging the Immune Synapse



Ritter A. *et al.*, *Immunity* 2015

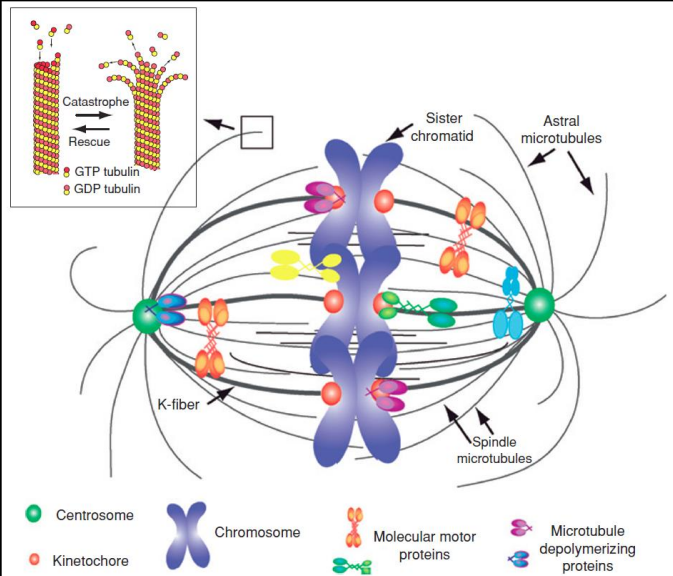
Technology

Applications

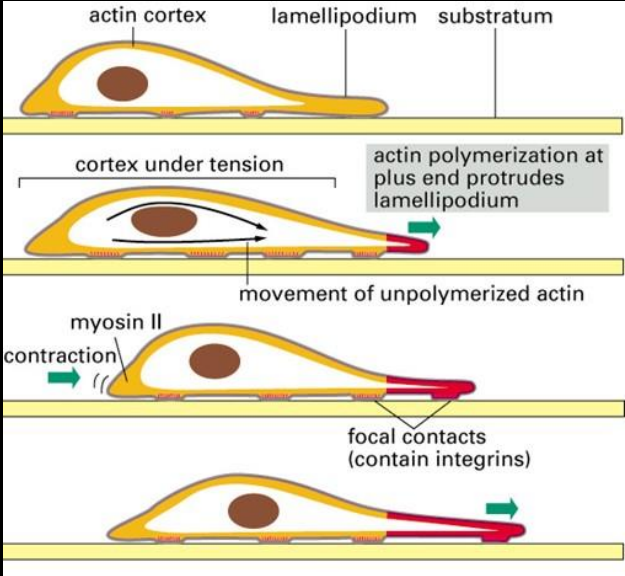
Collaborations

Future

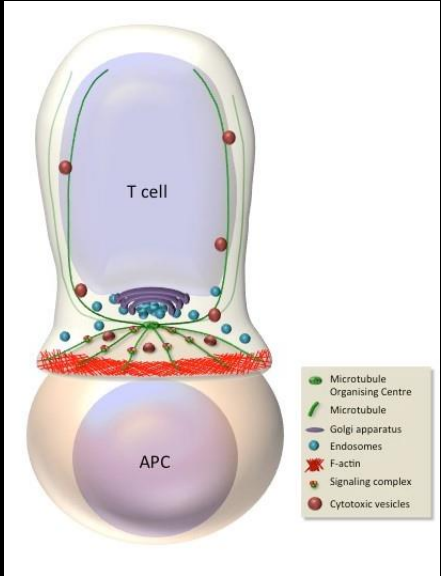
Animated Cell Biology – from Diagrams to Movies



Walczak C.E.. et al., *Int Rev Cytology* 2008

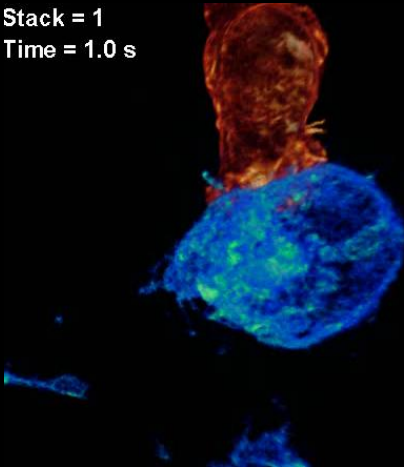
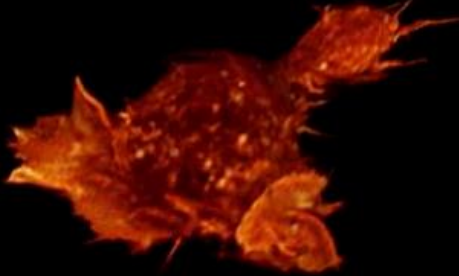
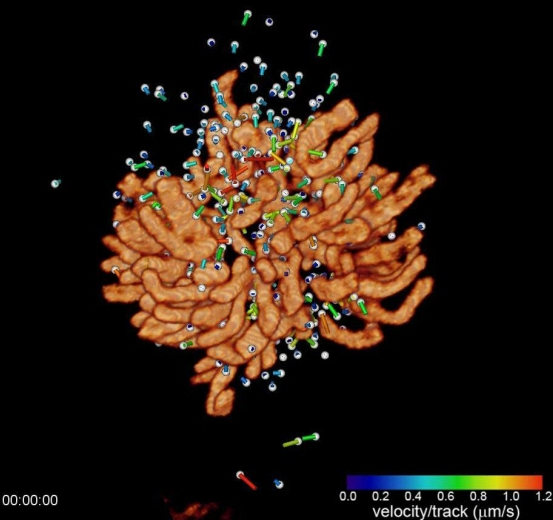


Molecular Biology of the Cell 2002



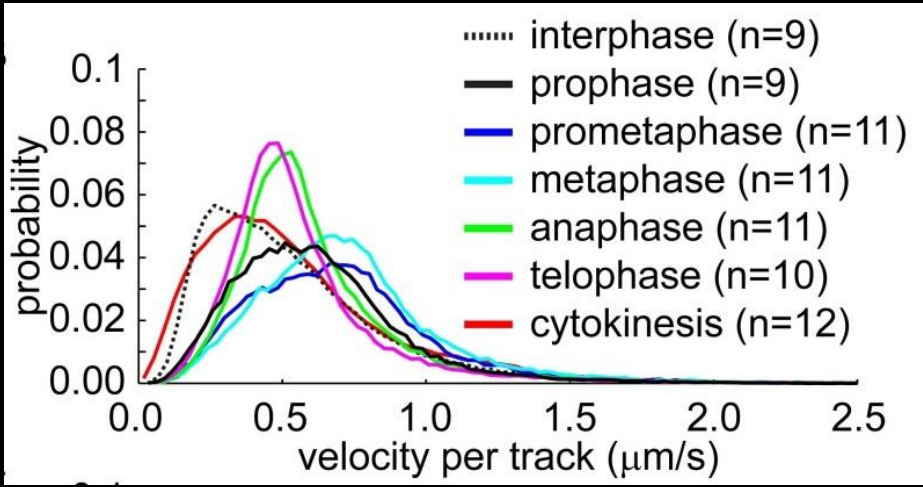
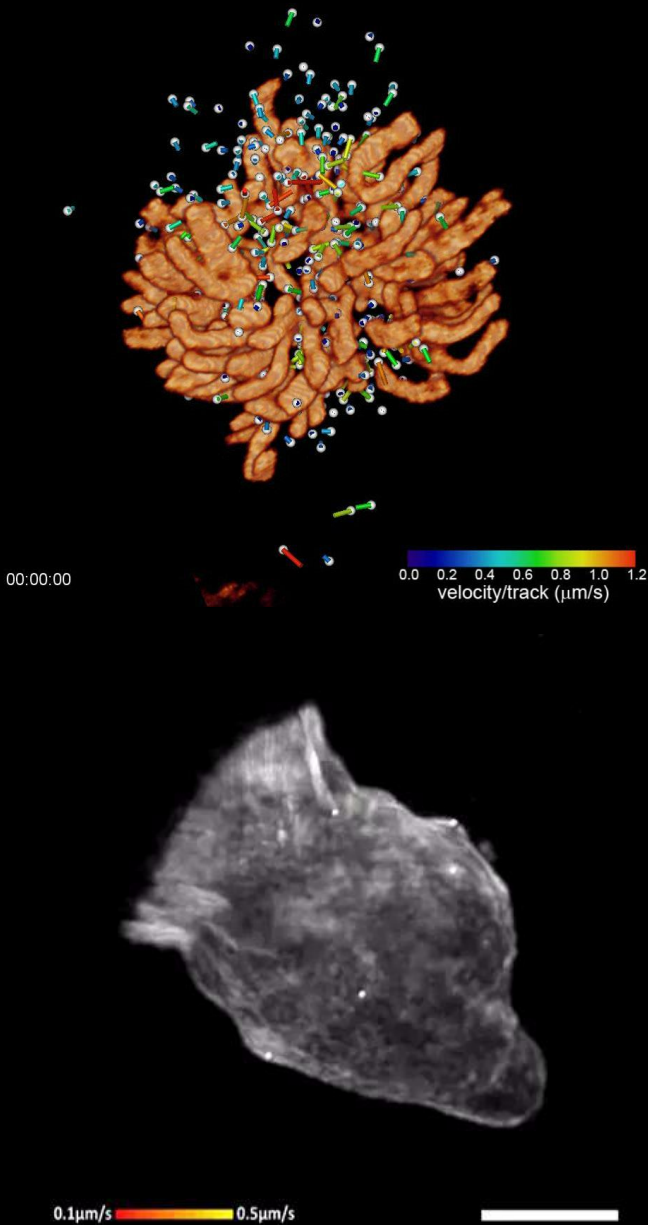
Alcover et al. 2018

prometaphase HeLa cell tracked GFP-EB1 tagRFP - H2B

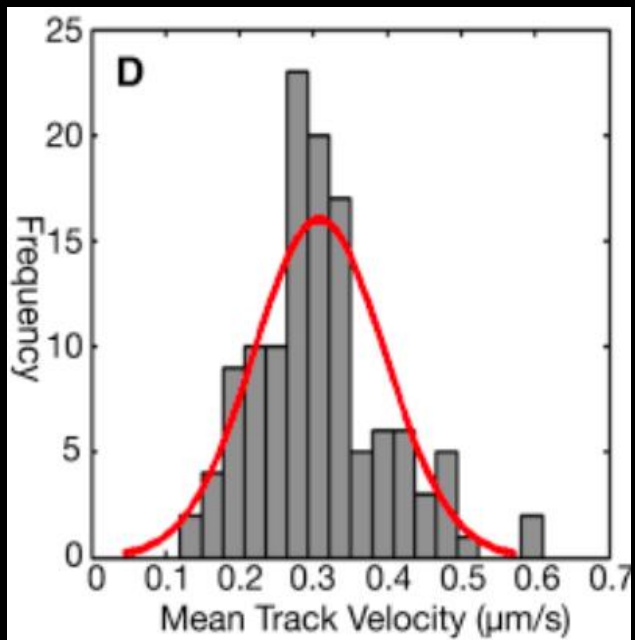


Quantitative Imaging – from Movies to Diagrams

prometaphase HeLa cell tracked GFP-EB1 tagRFP - H2B

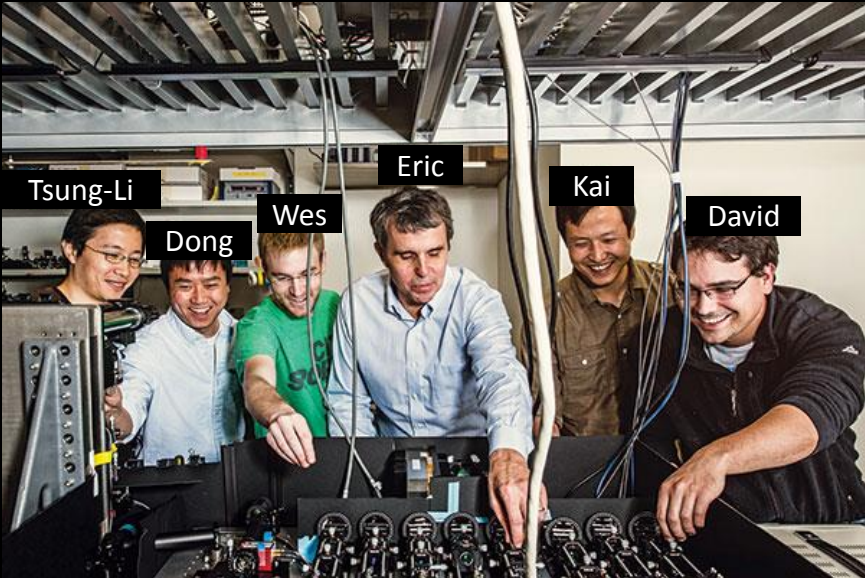


Code modified from Applegate K.T. *et al. J Struct Biol*, 2011



Ritter A. *et al., Immunity* 2015

Acknowledgements



Dan Milkie



Bi-Chang Chen

Janelia Research Campus



As of January 2018



Joint Department of
**BIOMEDICAL
ENGINEERING**



<http://legantlab.org>