Fiber optics emerging in circuit neuroscience

From single fibers to multi-fiber bundel arrays

Anna Maria Reuss
Technical Journal Club
30/04/2019

Fiber optics in a nut-shell

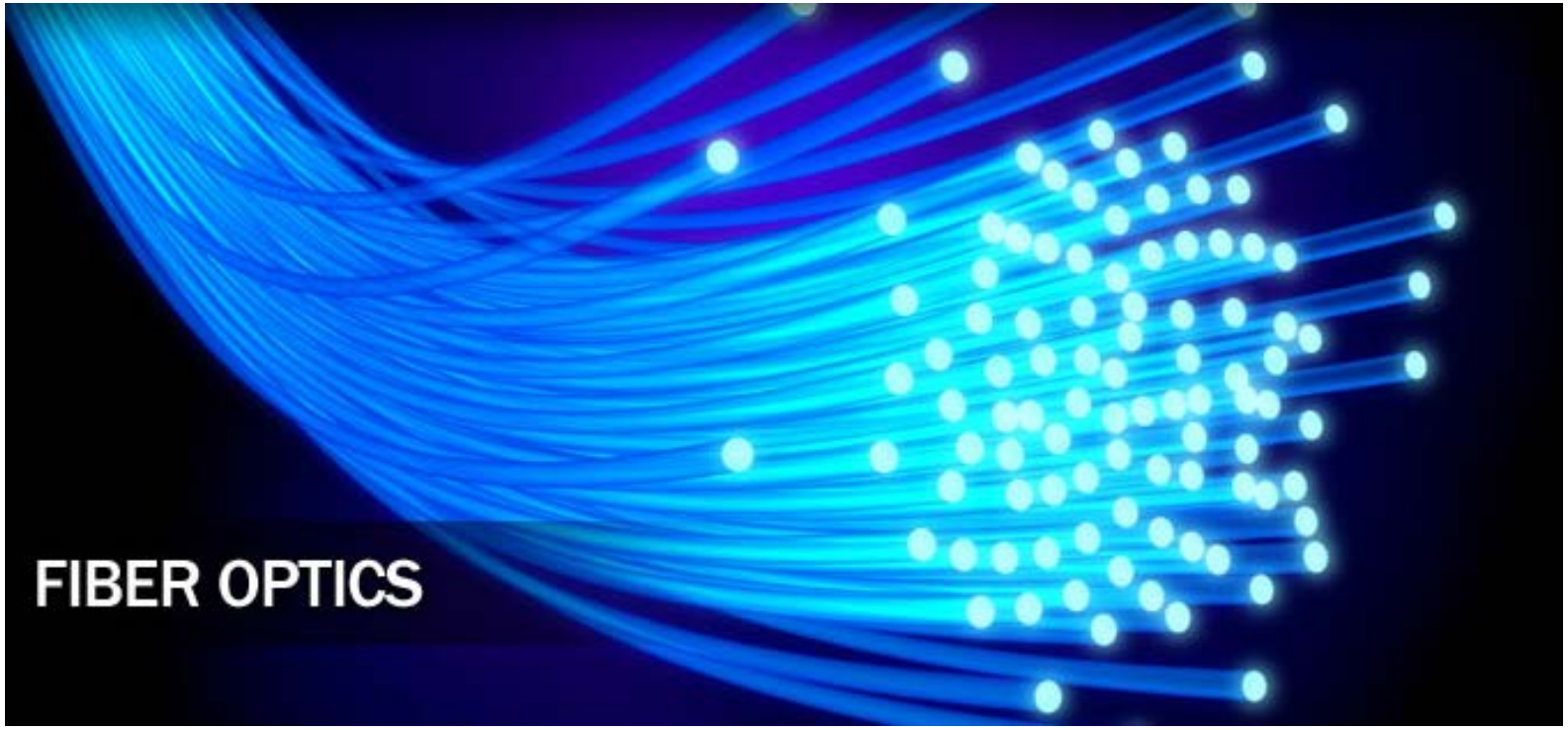
What is fiber optics?

How does a photometry setup look like?

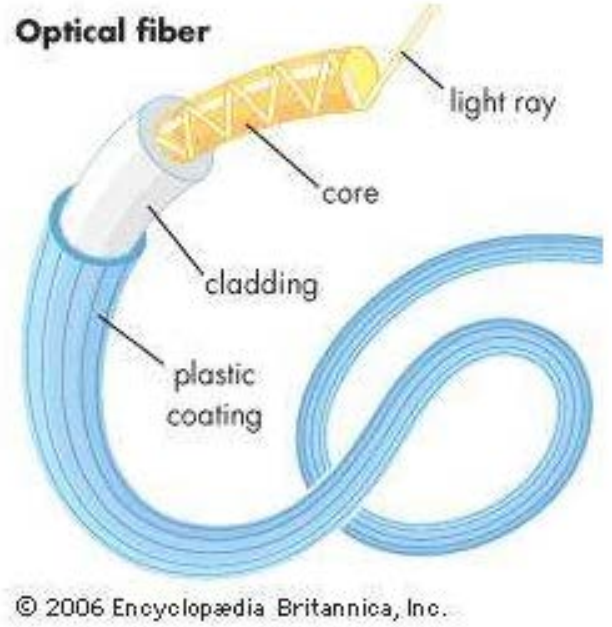
What is it used for in neuroscience?

Pros & cons of the technique

What is fiber optics?

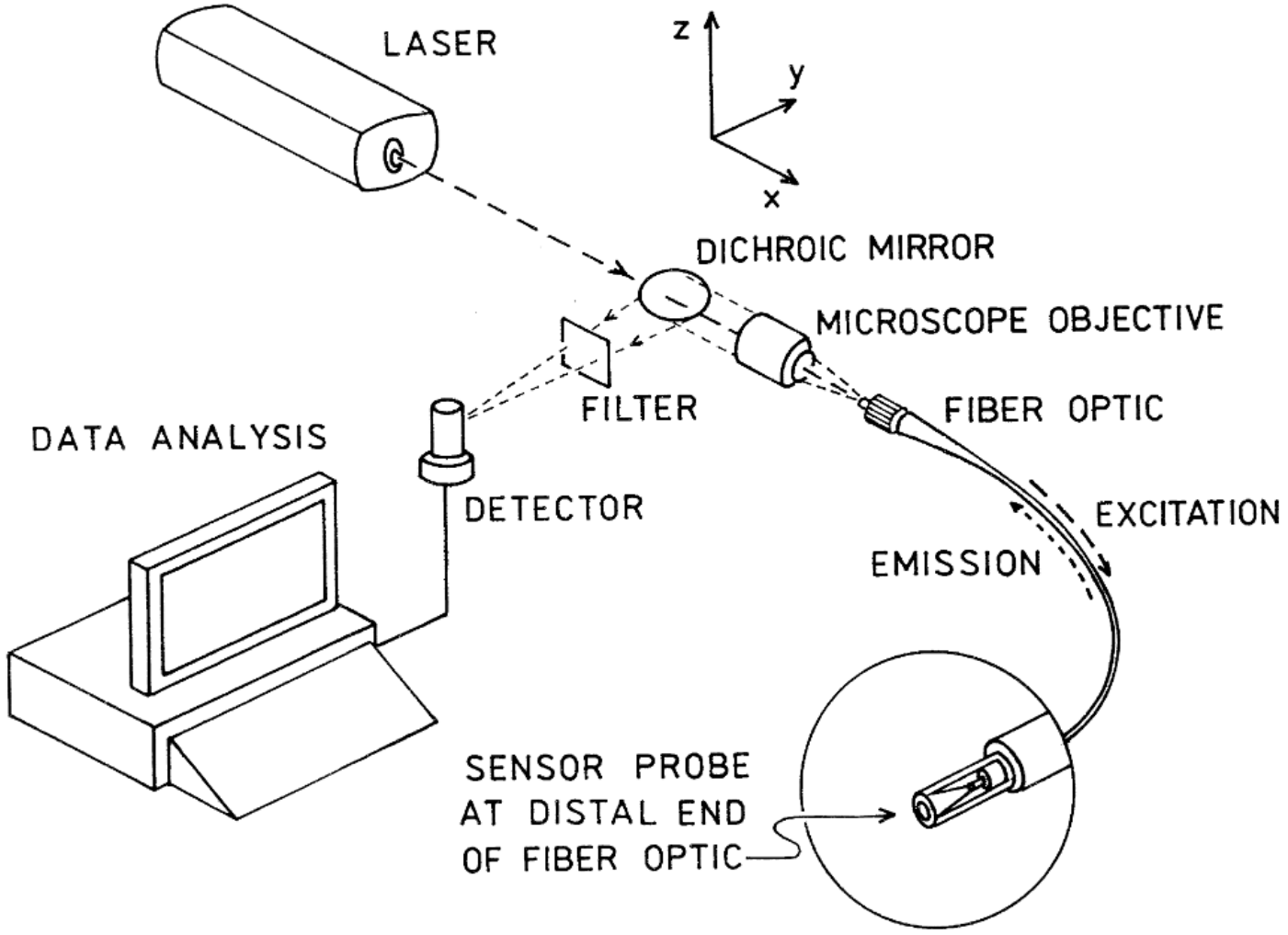


http://www.fugal.com/fiber-optics.html



YouTube/LearnEngineering

How does a photometry setup look like ?



Thompson et al., 2008

What can it be used for in neuroscience?

LETTER

doi:10.1038/nature17400

Nucleus accumbens D2R cells signal prior outcomes and control risky decision-making

Kelly A. Zalocusky[1,2,3], Charu Ramakrishnan[1,3], Talia N. Lerner[1,3], Thomas J. Davidson[1,3], Brian Knutson[4] & Karl Deisseroth[1,3,5]

BRIEF COMMUNICATIONS

Simultaneous fast measurement of circuit dynamics at multiple sites across the mammalian brain

Christina K Kim[1,8], Samuel J Yang[2,8], Nandini Pichamoorthy[3], Noah P Young[3], Isaac Kauvar[2], Joshua H Jennings[3], Talia N Lerner[3], Andre Berndt[3], Soo Yeun Lee[3], Charu Ramakrishnan[3], Thomas J Davidson[3], Masatoshi Inoue[4,5], Haruhiko Bito[4,5] & Karl Deisseroth[3,6,7]

High-density multi-fiber photometry for studying large-scale brain circuit dynamics

Yaroslav Sych[1,*], Maria Chernysheva[1,2], Lazar T. Sumanovski[1], and Fritjof Helmchen[1,2,*]

[1] Brain Research Institute, University of Zurich, Zurich, Switzerland
[2] Neuroscience Center Zurich, Zurich, Switzerland
*Correspondence should be addressed to Yaroslav Sych (sych@hifo.uzh.ch) and Fritjof Helmchen (helmchen@hifo.uzh.ch)

LETTER

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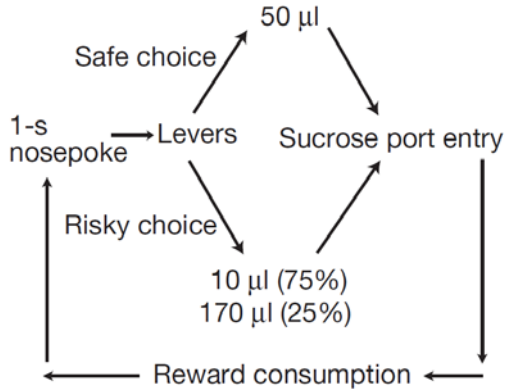
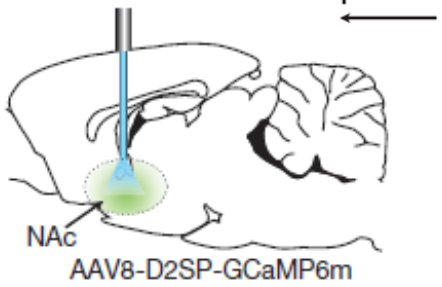
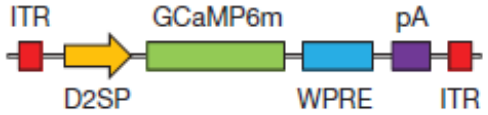
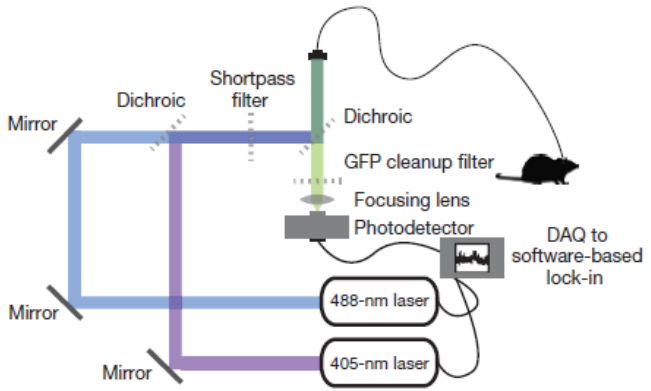
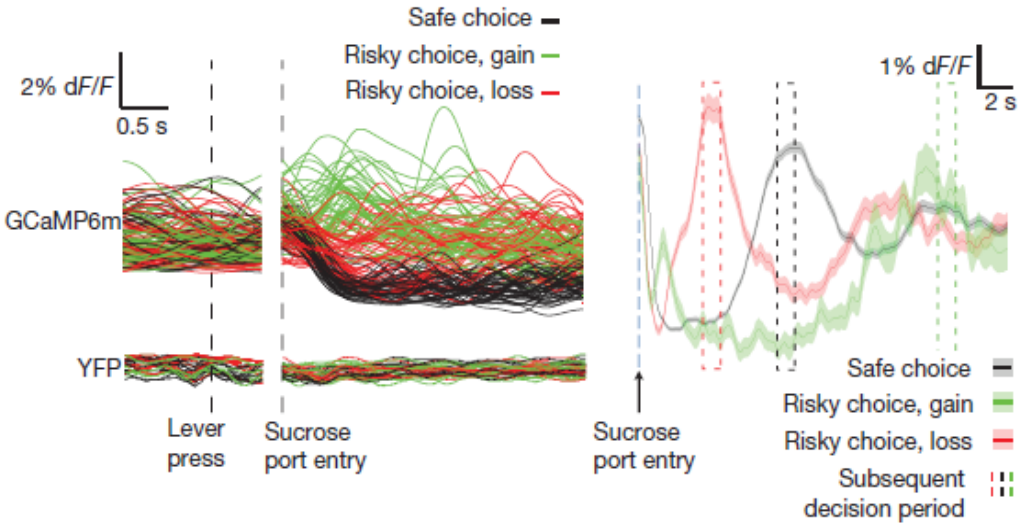
Zalocusky et al., 2016; Nature

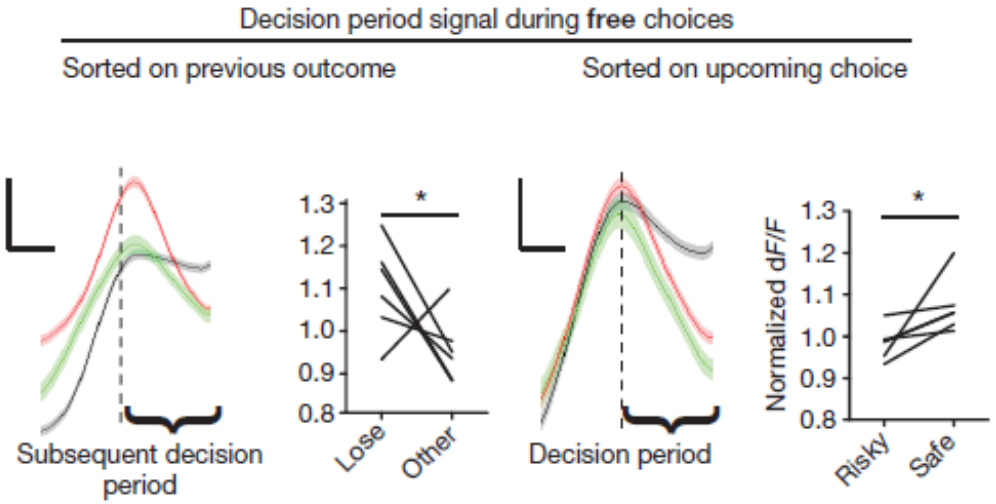

50 µl
Safe choice
1-s nosepoke
Levers
Sucrose port entry
Risky choice
10 µl (75%)
170 µl (25%)
Reward consumption

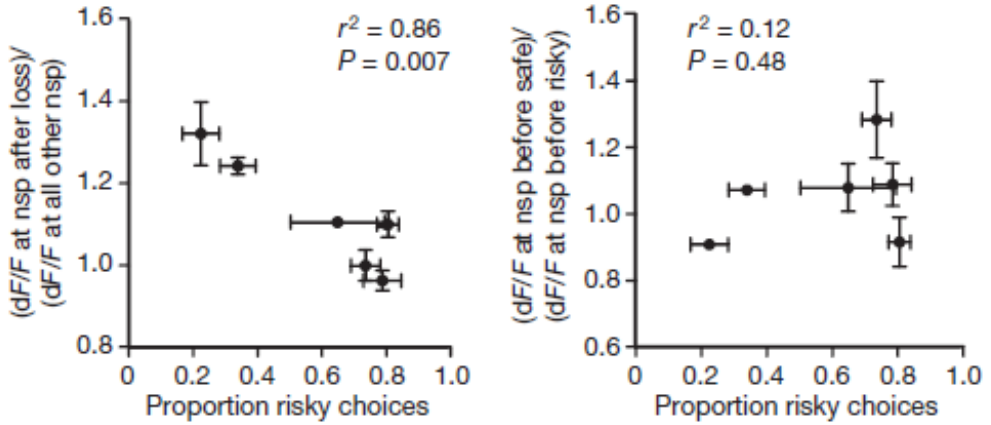

NAc
AAV8-D2SP-GCaMP6m


ITR
GCaMP6m
pA
D2SP
WPRE
ITR

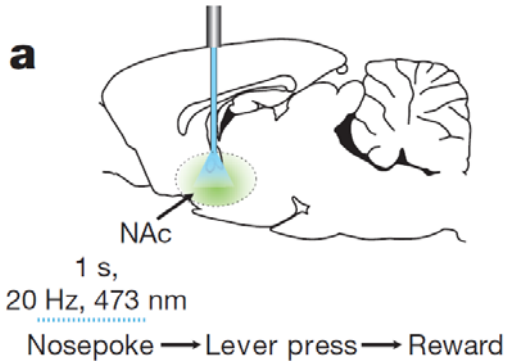

Mirror
Dichroic
Shortpass filter
Dichroic
GFP cleanup filter
Focusing lens
Photodetector
DAQ to software-based lock-in
Mirror
488-nm laser
Mirror
405-nm laser

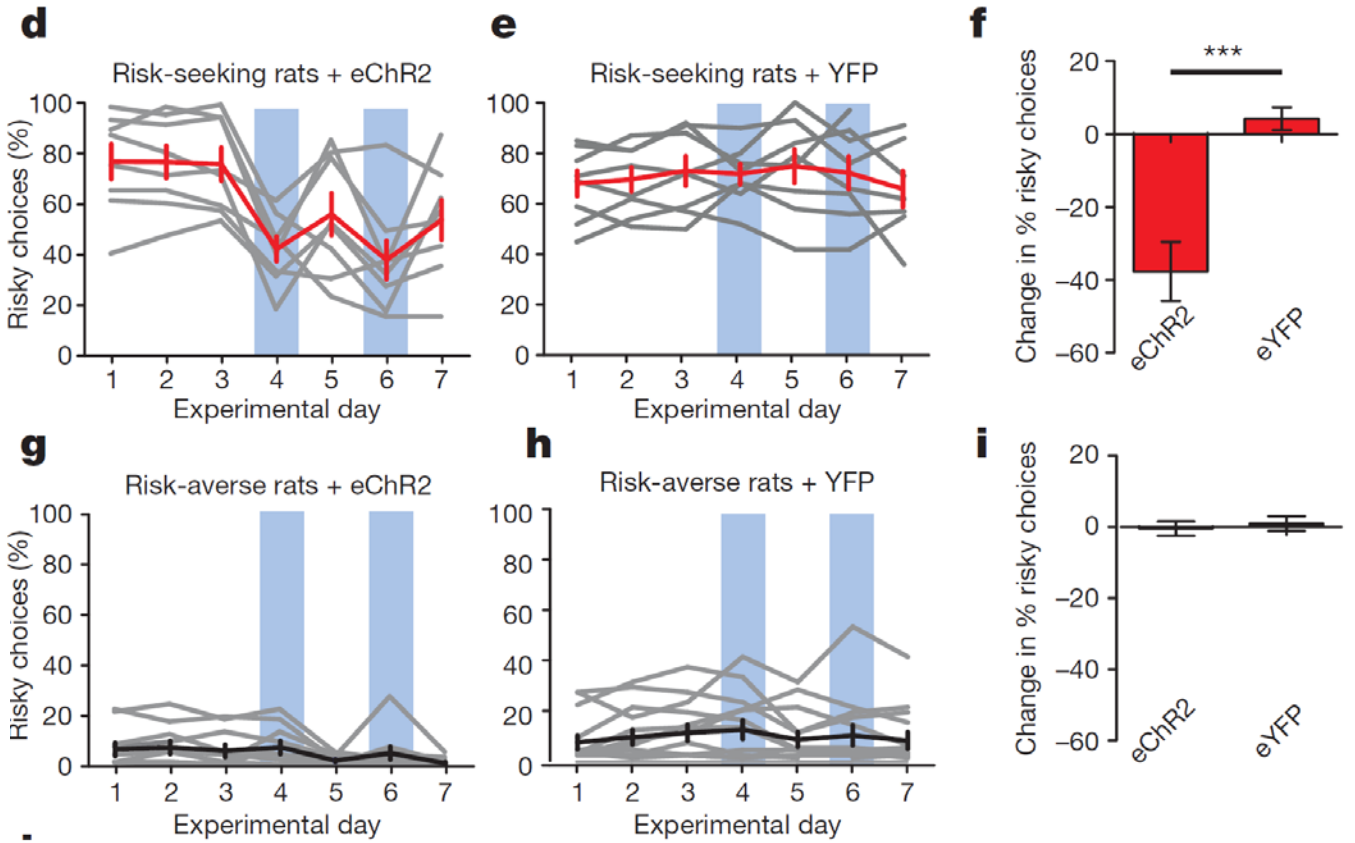

Safe choice
Risky choice, gain
Risky choice, loss
2% dF/F
0.5 s
GCaMP6m
YFP
Lever press
Sucrose port entry
1% dF/F
2 s
Sucrose port entry
Safe choice
Risky choice, gain
Risky choice, loss
Subsequent decision period

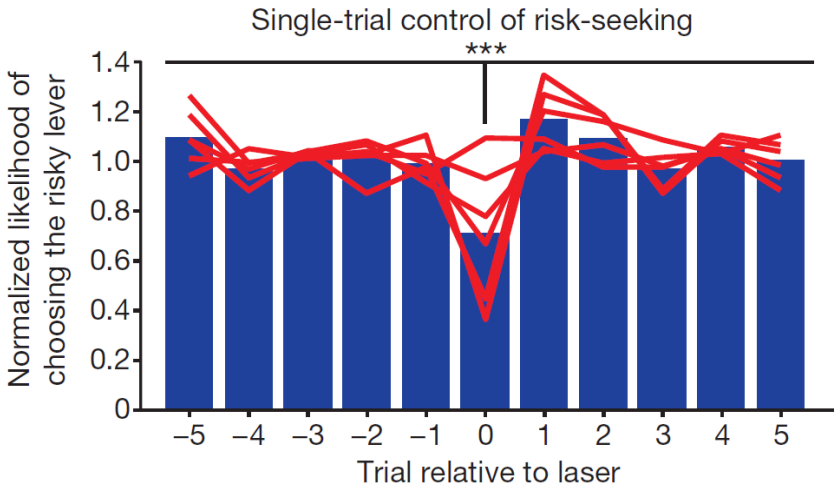

Decision period signal during free choices
Sorted on previous outcome
Sorted on upcoming choice
Subsequent decision period
Lose
Other
Decision period
Normalized dF/F
Risky
Safe


r² = 0.86
P = 0.007
(dF/F at nsp after loss)/ (dF/F at all other nsp)
Proportion risky choices
r² = 0.12
P = 0.48
(dF/F at nsp before safe)/ (dF/F at nsp before risky)
Proportion risky choices

Using optogenetics to provide phasic activity in D2-expressing NAc cells during the decision period







Conclusions

- Technique allows to identify relevant temporally specific signals from a genetically and anatomically defined population of neurons
- D2 neurons in the NAc signal unfavourable outcomes from the recent past at a time appropriate for influencing subsequent decisions
- Risk-preferring rats can be converted to risk-averse rats with precisely timed phasic stimulation of NAc D2R cells
- Individual differences in risk-preference as well as real-time risky decision-making can be largely explained by the encoding in D2R-expressing NAc cells of prior unfavourable outcomes during decision-making

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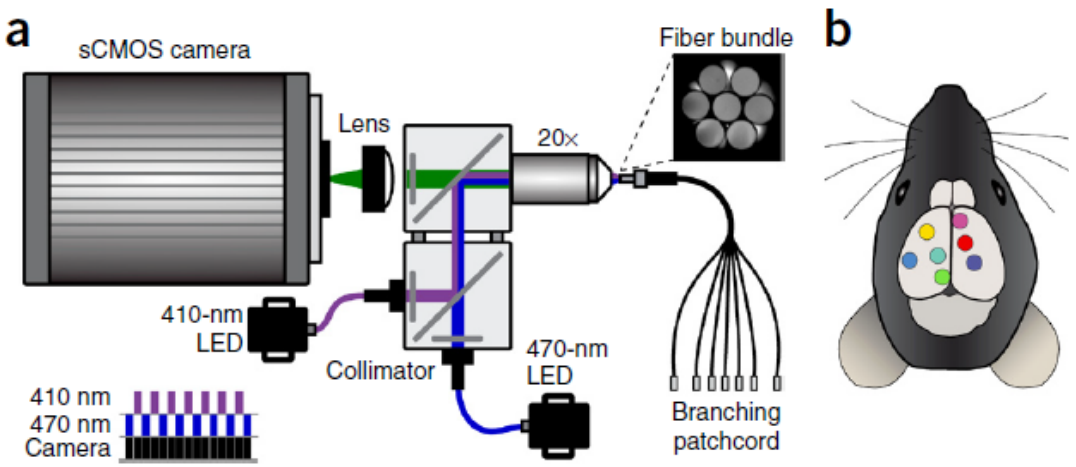
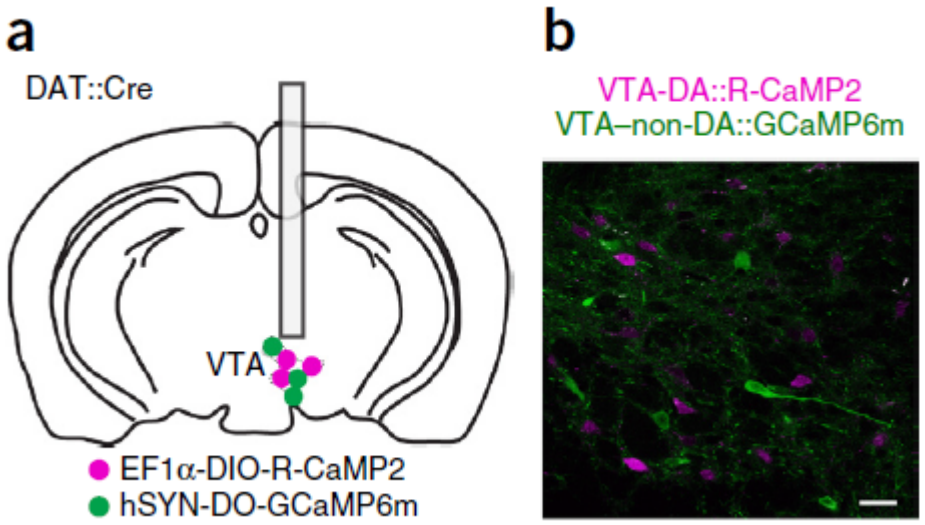
Kim et al., 2016; Nature Methods


a
sCMOS camera
Lens
20×
Fiber bundle
410-nm
LED
Collimator
470-nm
LED
410 nm
470 nm
Camera
Branching
patchcord
b


a
DAT::Cre
VTA
EF1α-DIO-R-CaMP2
hSYN-DO-GCaMP6m
b
VTA-DA::R-CaMP2
VTA–non-DA::GCaMP6m

Conclusions

- Multiple-channel recordings from different brain regions and different cell populations
- Simultaneous recordings from cell bodies (VTA) and axonal projections
- Dual-color photometry through one fiber
- Combination of photometry and optogenetics through one fiber

- Problems:
  - Mostly only one mouse and very few trials per experiment
  - $\Delta F/F$ scales different for comparisons
  - Equal light distribution into the different fibers?

High-density multi-fiber photometry for studying large-scale brain circuit dynamics

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[2] Neuroscience Center Zurich, Zurich, Switzerland
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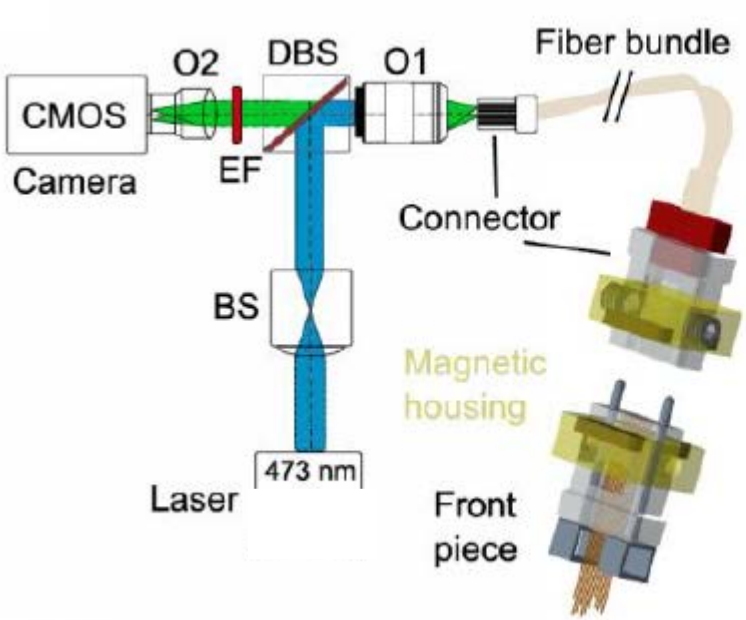
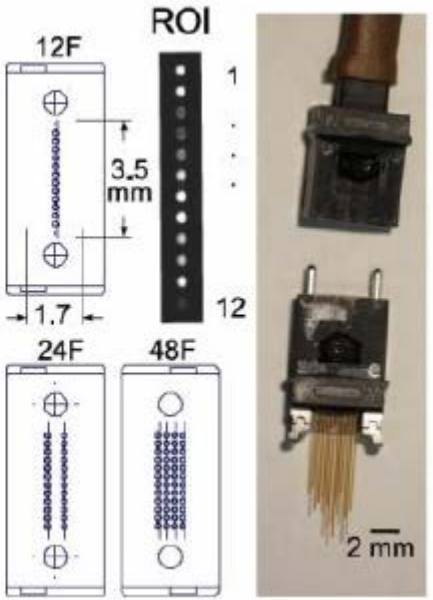
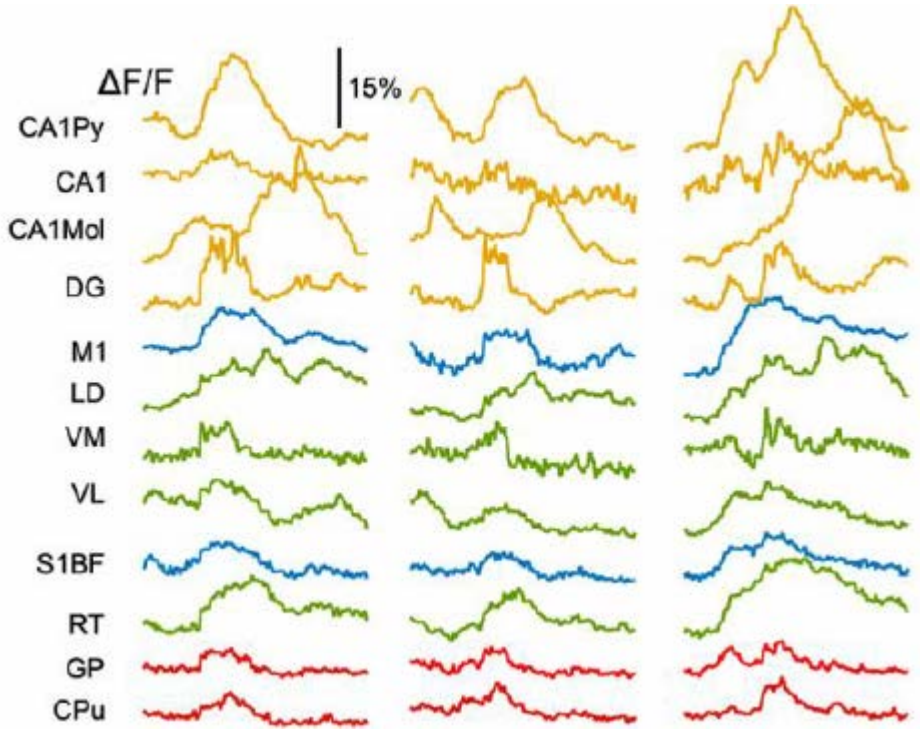
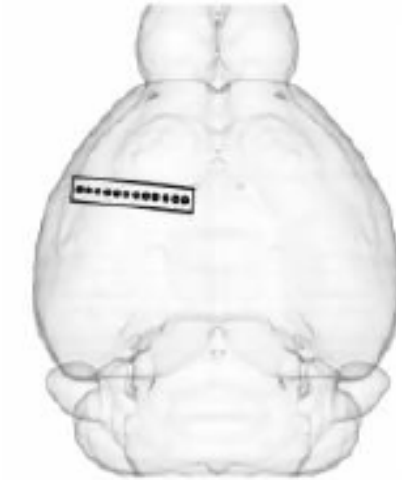
Sych et al., 2019; Nature Methods accepted

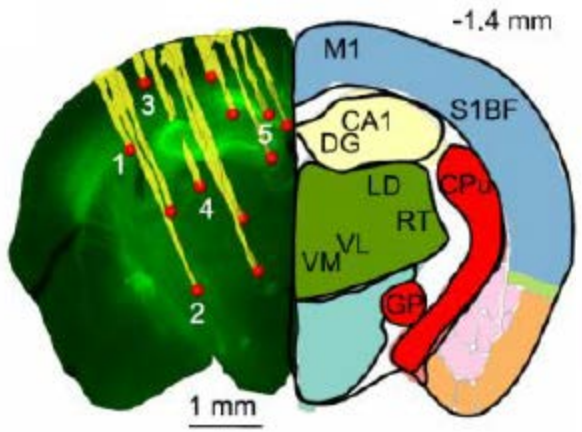

O2
DBS
O1
Fiber bundle
CMOS
Camera
EF
Connector
BS
Magnetic
housing
473 nm
Laser
Front
piece

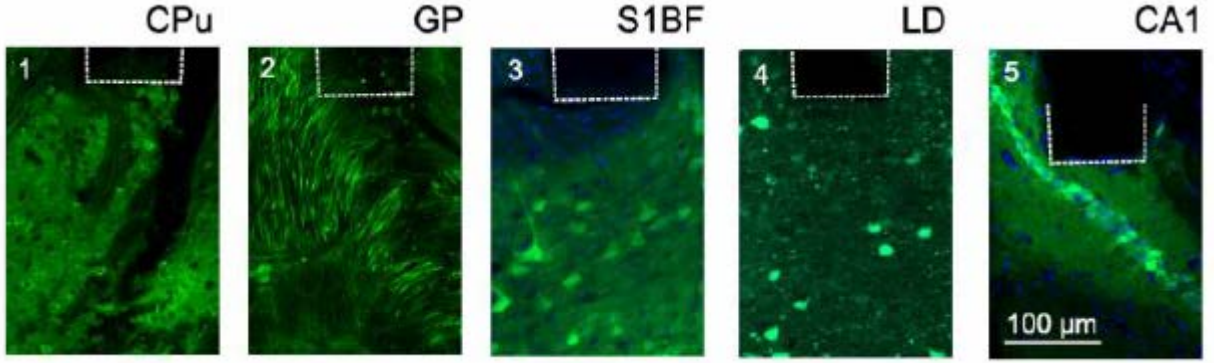

12F
ROI
1
3.5
mm
12
1.7
24F
48F

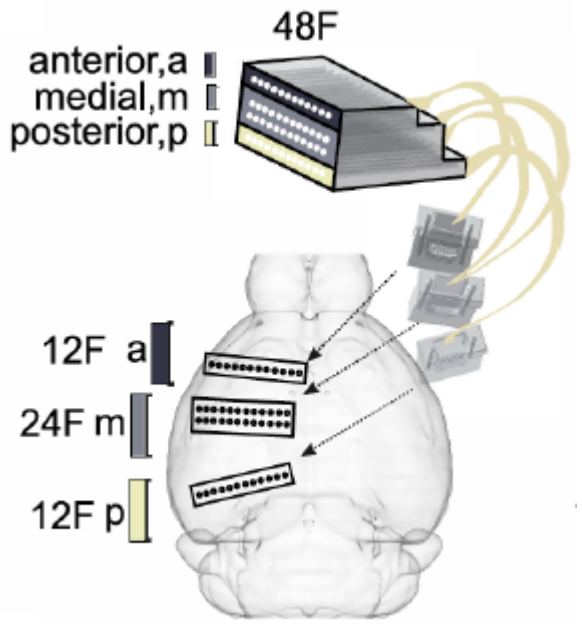
2 mm

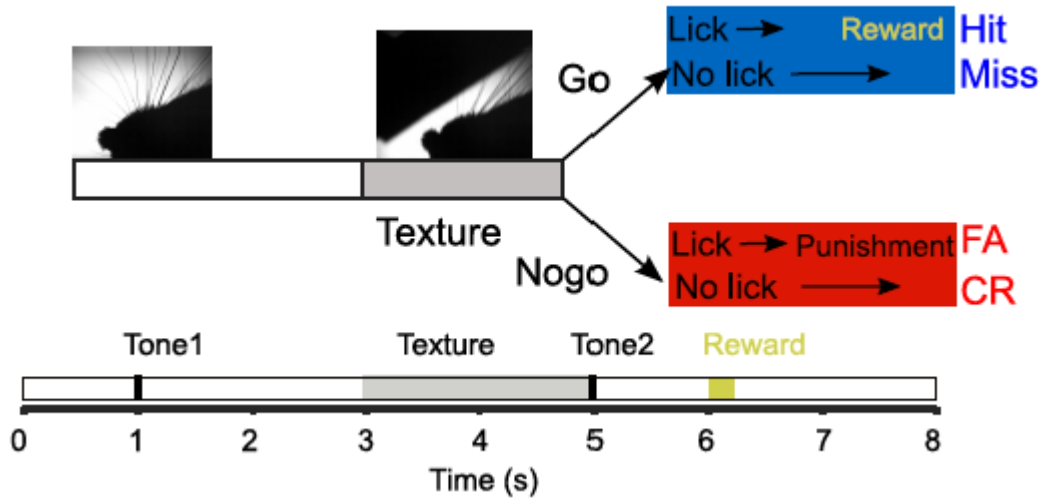

ΔF/F
15%
CA1Py
CA1
CA1Mol
DG
M1
LD
VM
VL
S1BF
RT
GP
CPu

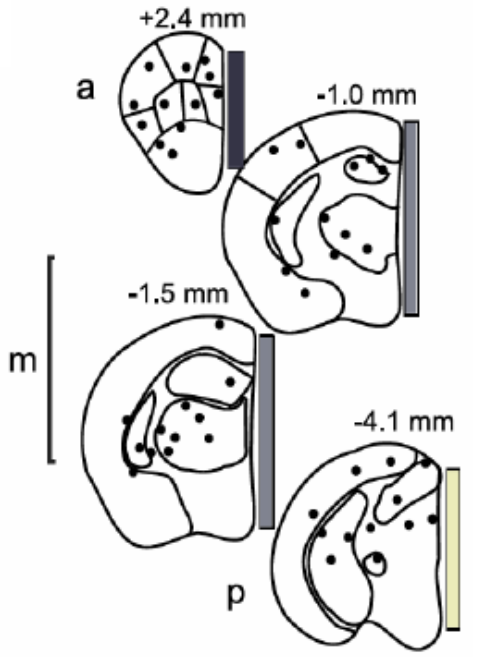


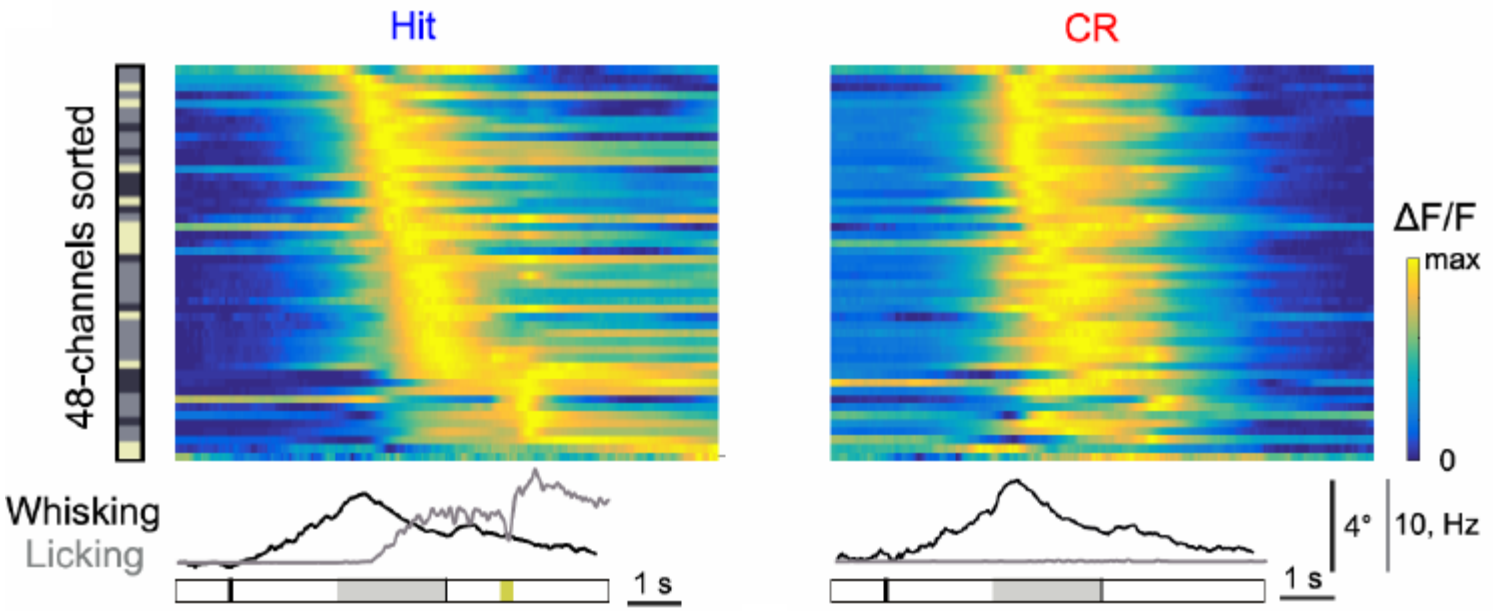

-1.4 mm
M1
S1BF
CA1
DG
LD
CPu
RT
VM
VL
GP
1
2
3
4
5
1 mm

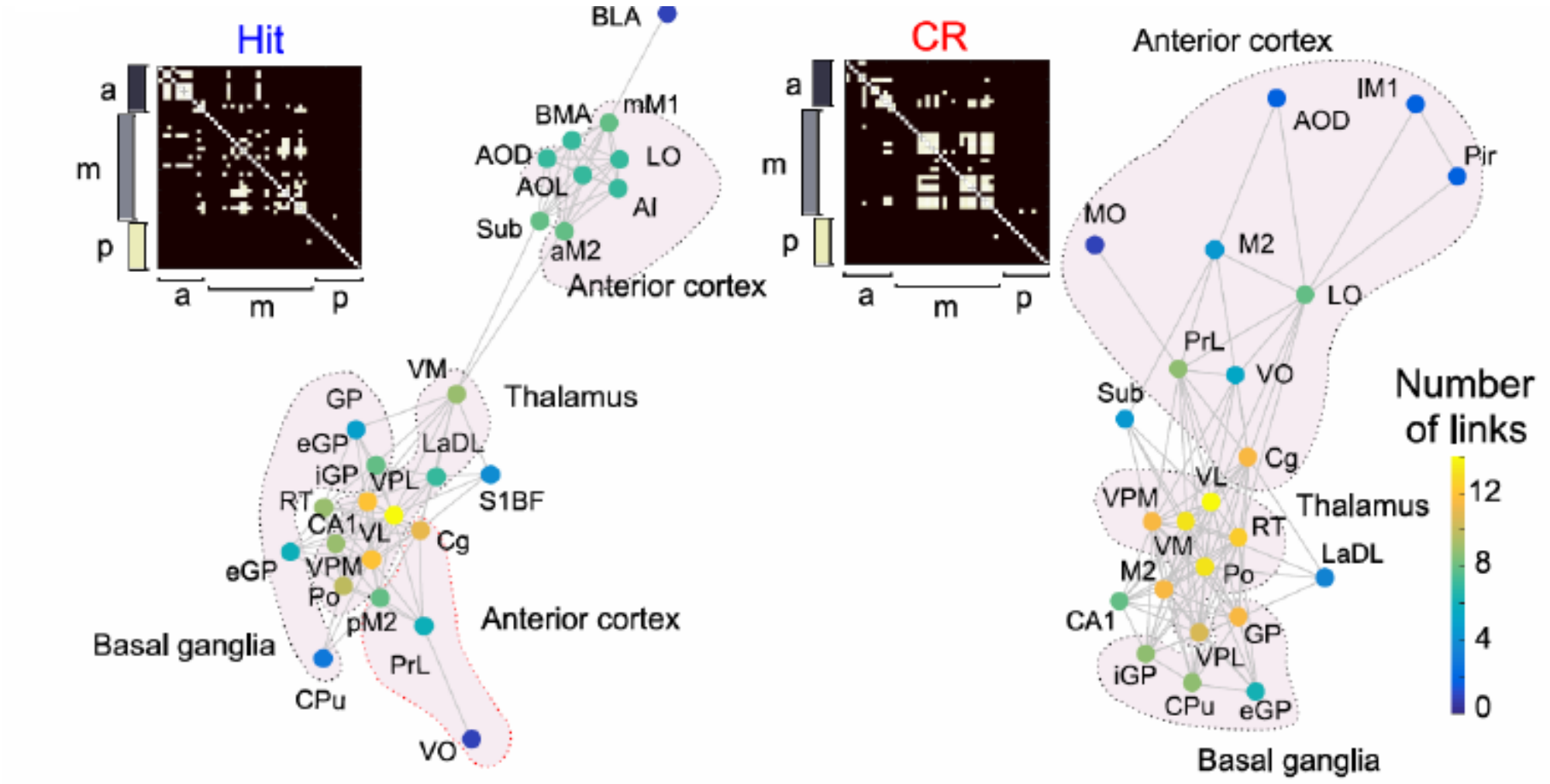

CPu
GP
S1BF
LD
CA1
1
2
3
4
5
100 µm


48F
anterior,a
medial,m
posterior,p
12F a
24F m
12F p

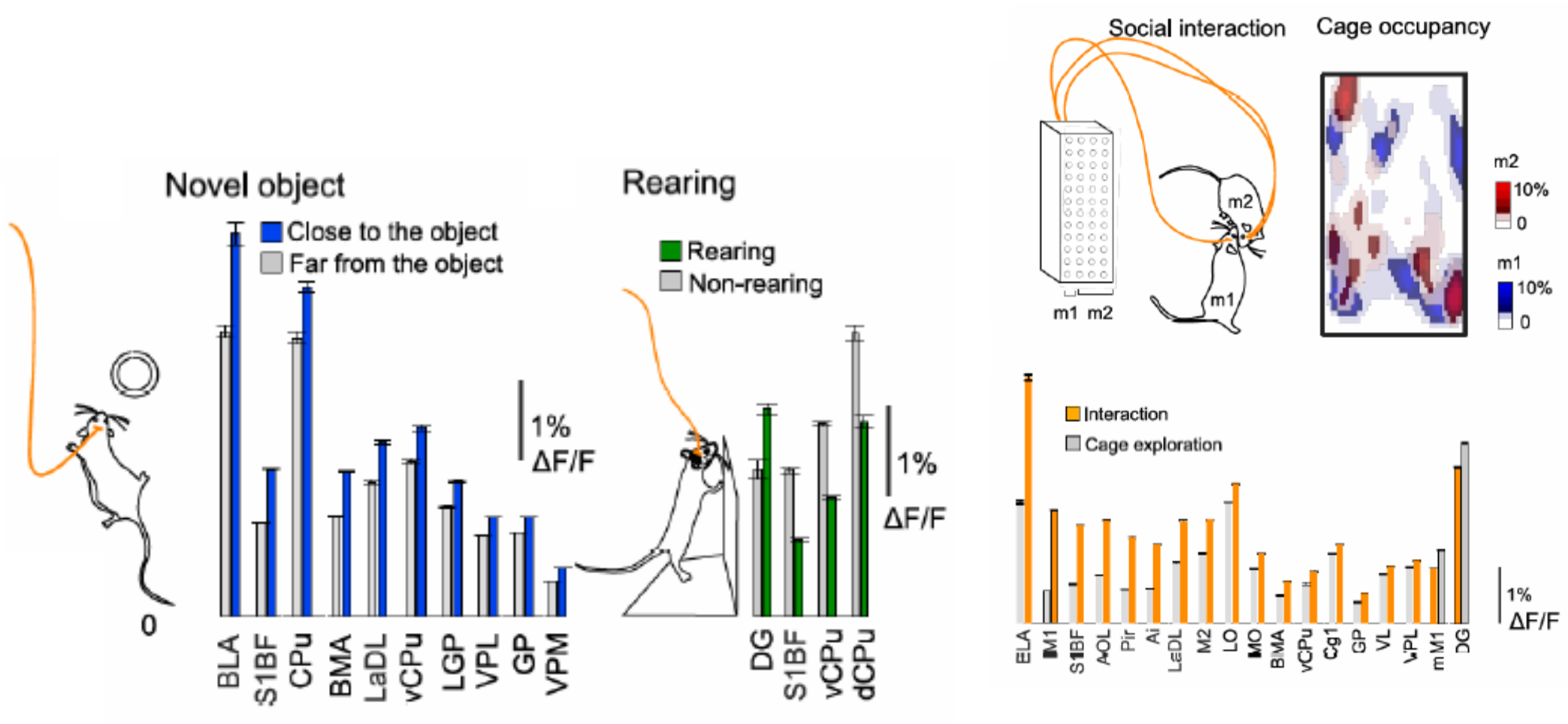

Go
Lick
Reward
Hit
No lick
Miss
Texture
Nogo
Lick
Punishment
FA
No lick
CR
Tone1
Texture
Tone2
Reward
0
1
2
3
4
5
6
7
8
Time (s)


+2.4 mm
a
-1.0 mm
-1.5 mm
m
-4.1 mm
p

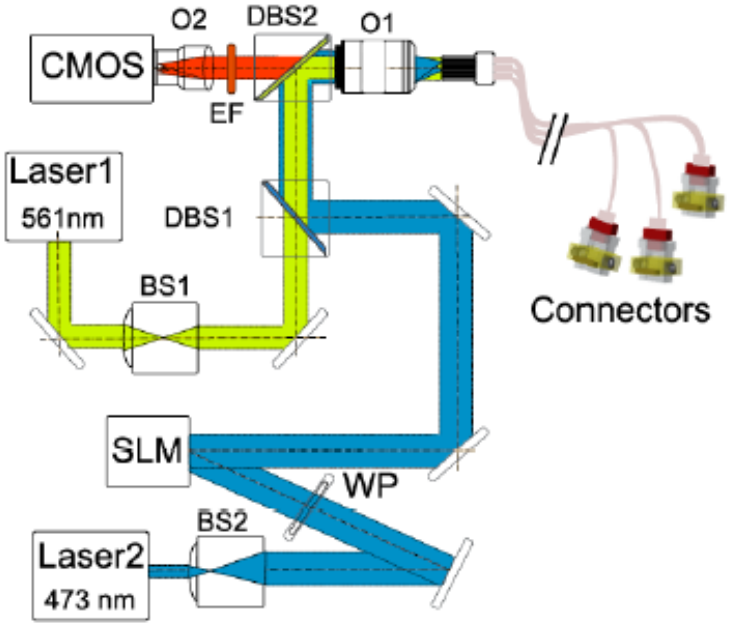

Hit
CR
48-channels sorted
ΔF/F
max
0
Whisking
Licking
1 s
1 s
4°
10, Hz

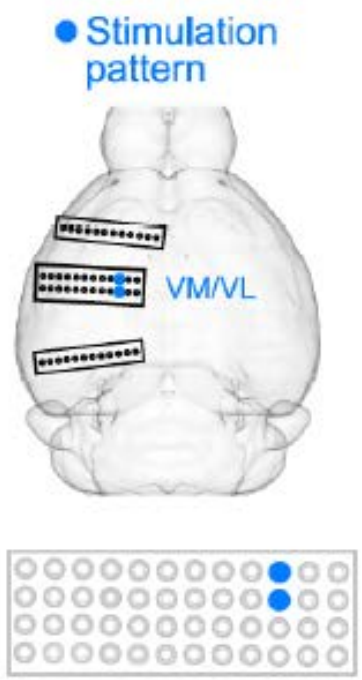

Hit
a
m
p
a
m
p
BLA
BMA
mM1
AOD
LO
AOL
AI
Sub
aM2
Anterior cortex
VM
GP
Thalamus
eGP
LaDL
iGP
VPL
S1BF
RT
CA1
VL
Cg
eGP
VPM
Po
pM2
Anterior cortex
Basal ganglia
PrL
CPu
VO
CR
a
m
p
a
m
p
Anterior cortex
IM1
AOD
Pir
MO
M2
LO
PrL
VO
Sub
Cg
VL
VPM
Thalamus
RT
VM
LaDL
M2
Po
CA1
GP
VPL
iGP
CPu
eGP
Basal ganglia
Number of links
12
8
4
0

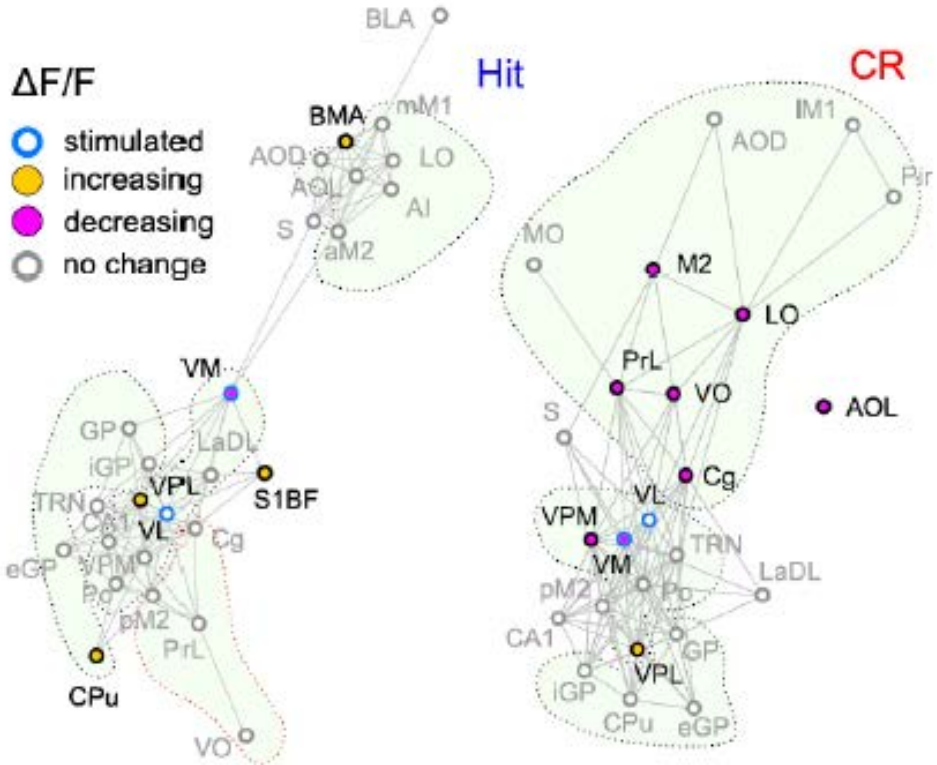
High density fiber bundels recordings can be performed in freely moving animals



High density fiber bundels allows simultaneous multi-region calcium recordings during optogenetics perturbation of single regions







Conclusions

- Up to 48 channels recordings over many brain regions
- Creation of functional networks
- In freely-moving animals
- Optogenetic perturbation and simultaneous recordings of whole networks

Pros & Cons

Pro

- **Simplicity**
- **Minimum head weight**
- **Negligible heat generation**
- **Cost-efficiency**
- **Potential fast acquisition rate**
- **Customizable fibers**
- **Reduced invasiveness**
- **Easy combination with optogenetics**
- **Long-term experiments**

Contra

- **(Still) invasive**
- **Limited spatial information**
- **Connection to fiber-bundle necessary (alternative: wire-less LED modules)**

Thank you for your attention!

https://www.zerotoys.com/GLACIER-LITE-p/glacierlite.htm