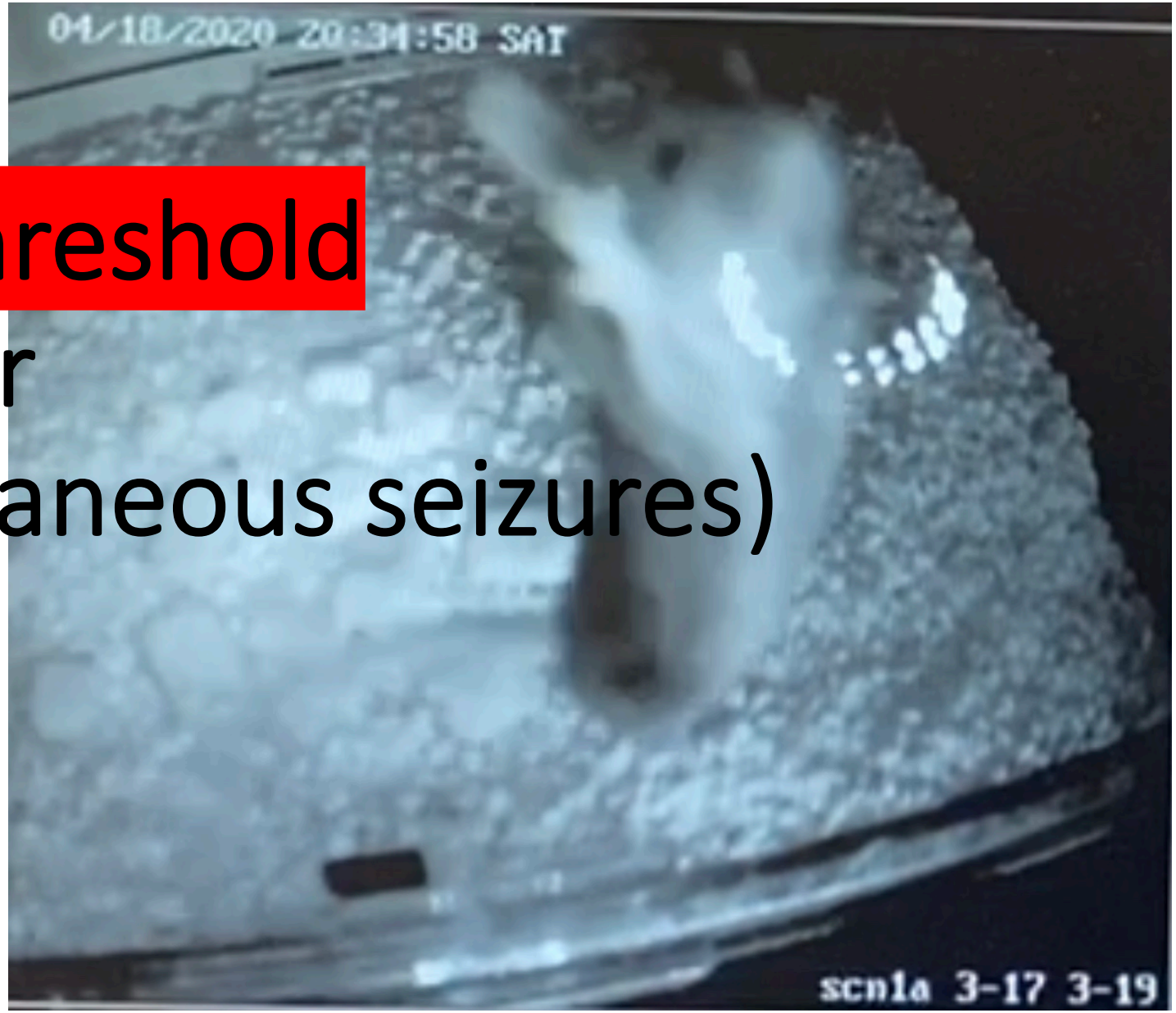
Is Temperature Threshold a reliable indicator of sickness (spontaneous seizures) in epileptic mice?



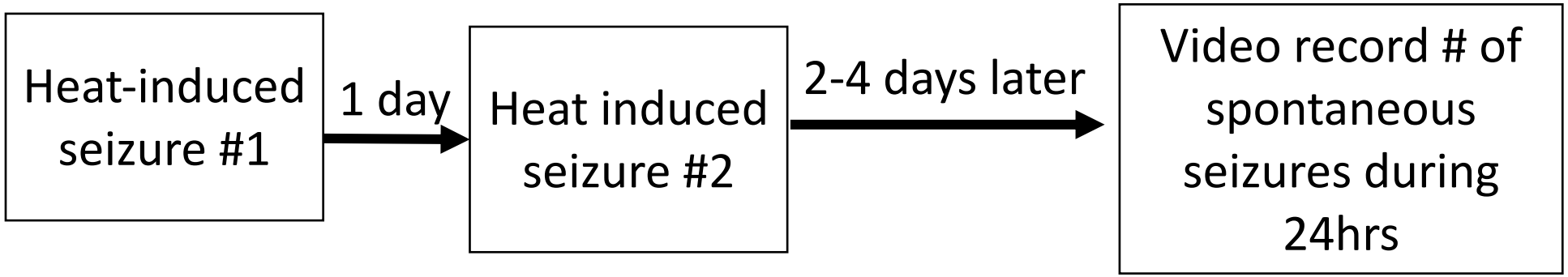
Nate Sotuyo
Co-advisors:
Stewart Anderson and Ethan Goldberg

NGG Data presentation

Experimental paradigm

Two days of heat-induced seizures:
Output measure: rectal temperature
(threshold at which seizure occurs)

Output measure #2:
# of spontaneous seizures
(during 24hrs)



But, which measurements matter?

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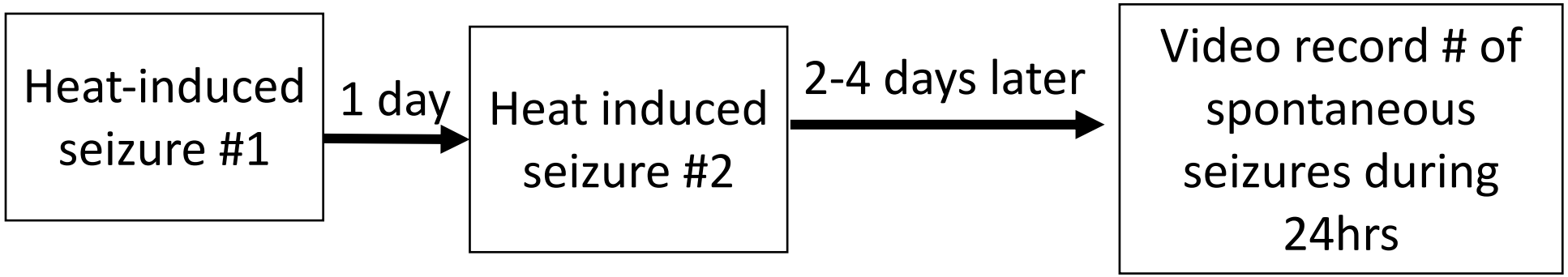

But, which measurements *matter*?

1. **Nate needs a PhD** (i.e. the measurement should be possible).
    1. Temperature threshold is ”easy” to measure
    2. Spontaneous seizures may be “easy” to measure, BUT…
        1. The measurement prohibitively time-intensive
        2. Most mutant mice don’t actually have seizures…

2. **Measurements should be biologically me**
    1. Spontaneous seizure frequency inhe
    2. A lower ”Seizure threshold” == a se
    3. There is no evidence that the sickest ature thresholds.
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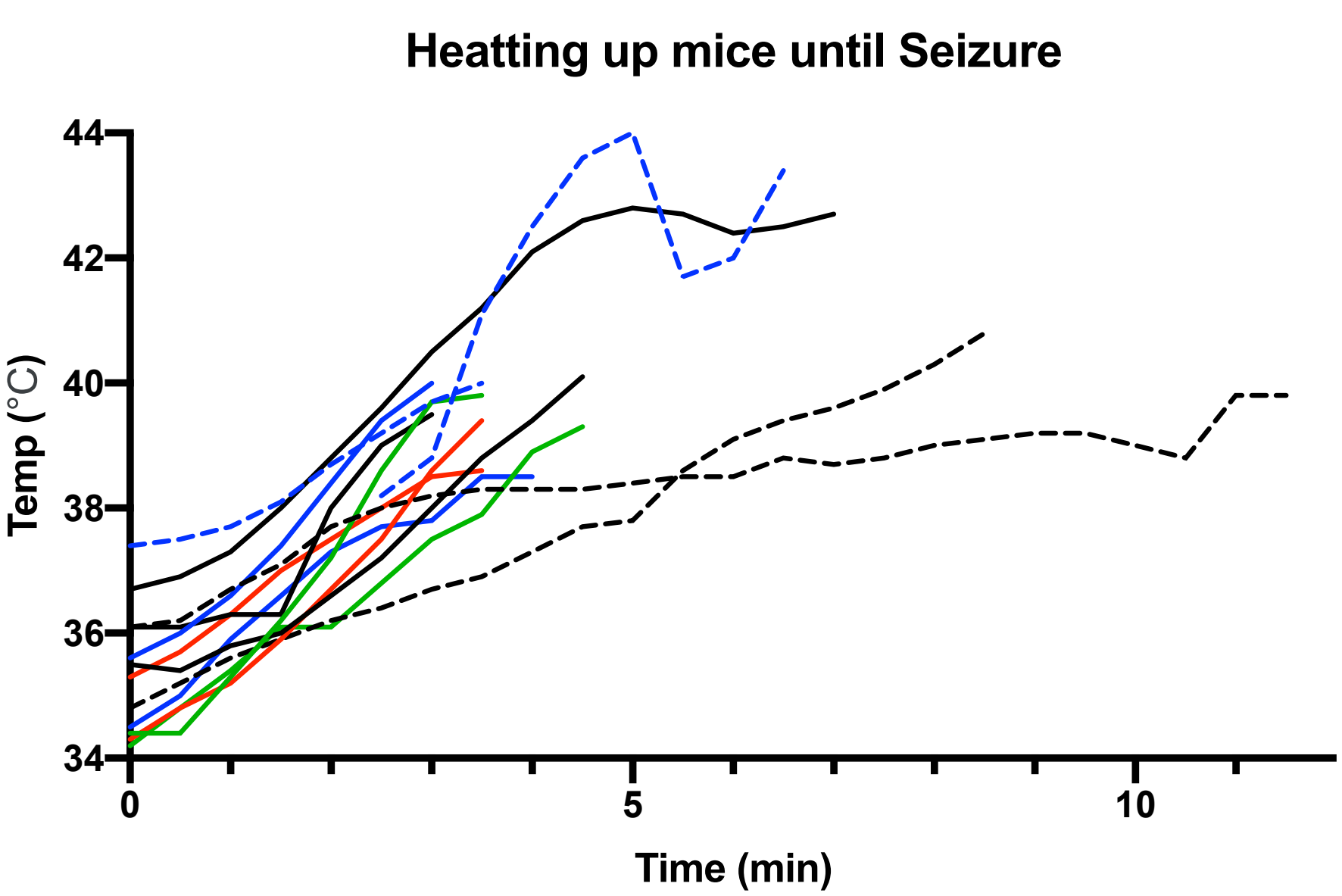
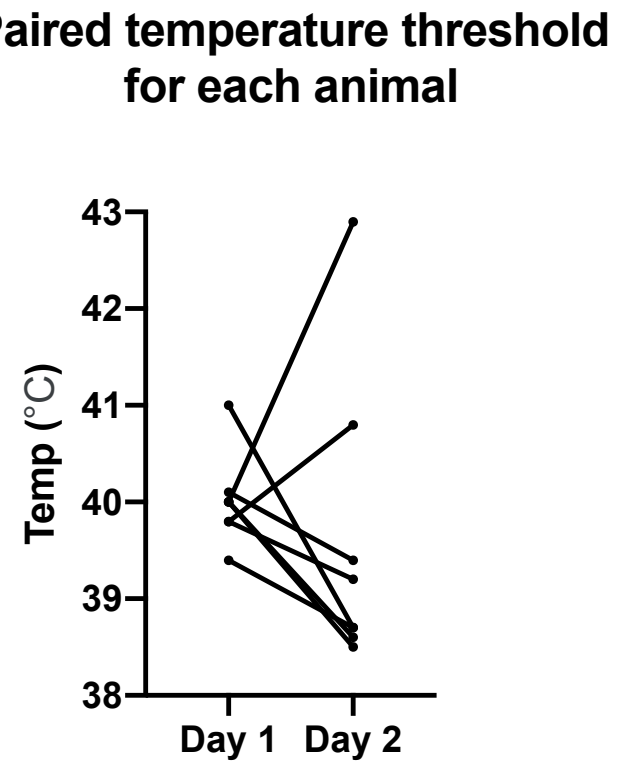
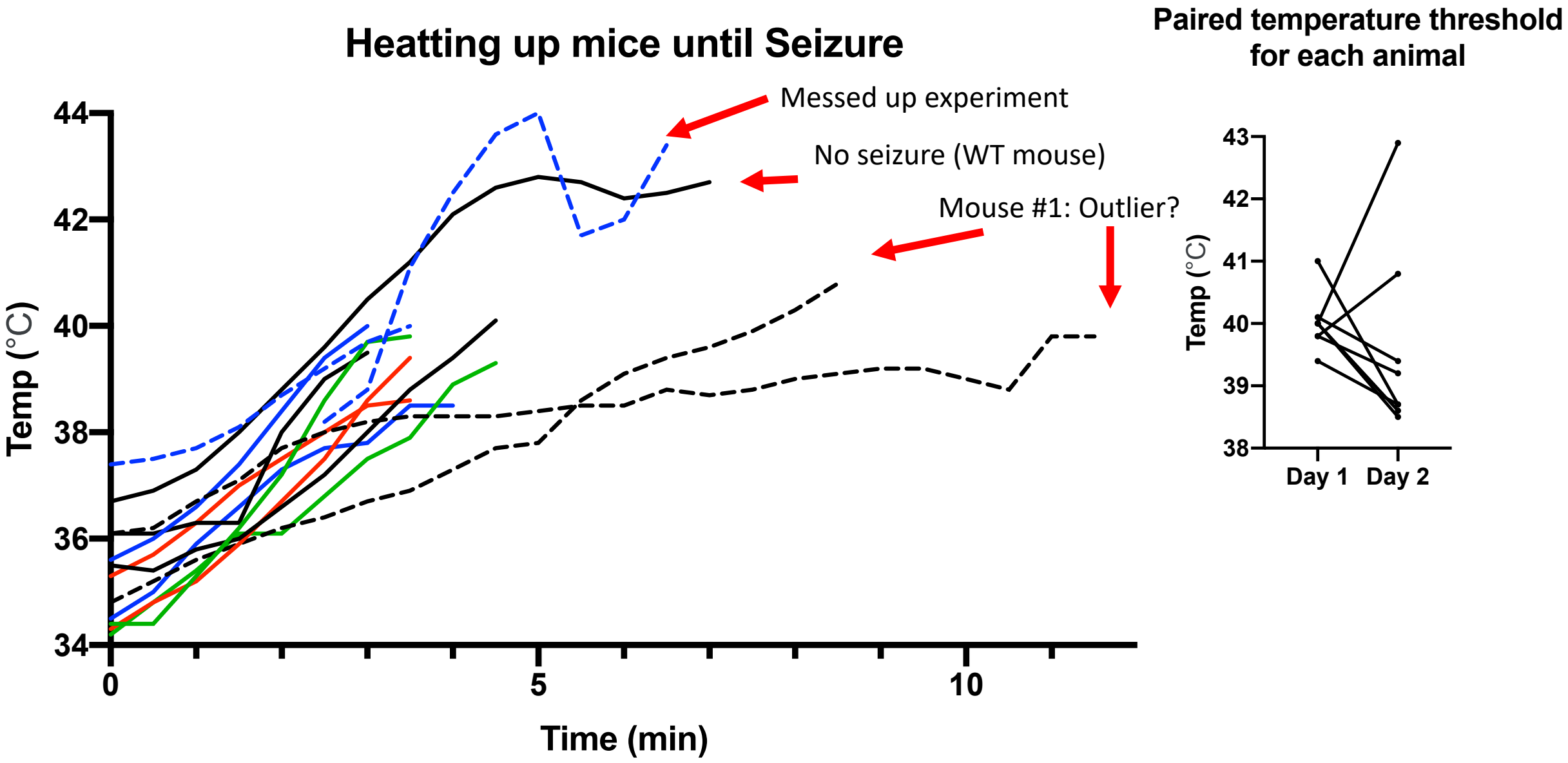
Charlotte Figi: Oct. 18, 2006 -- April 7, 2020


Heatting up mice until Seizure
Temp (°C)
44
42
40
38
36
34
0
5
10
Time (min)


Paired temperature threshold for each animal
Temp (°C)
43
42
41
40
39
38
Day 1
Day 2


Heatting up mice until Seizure
Messed up experiment
No seizure (WT mouse)
Mouse #1: Outlier?
Temp (°C)
44
42
40
38
36
34
0
5
10
Time (min)
Paired temperature threshold for each animal
Temp (°C)
43
42
41
40
39
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Day 1
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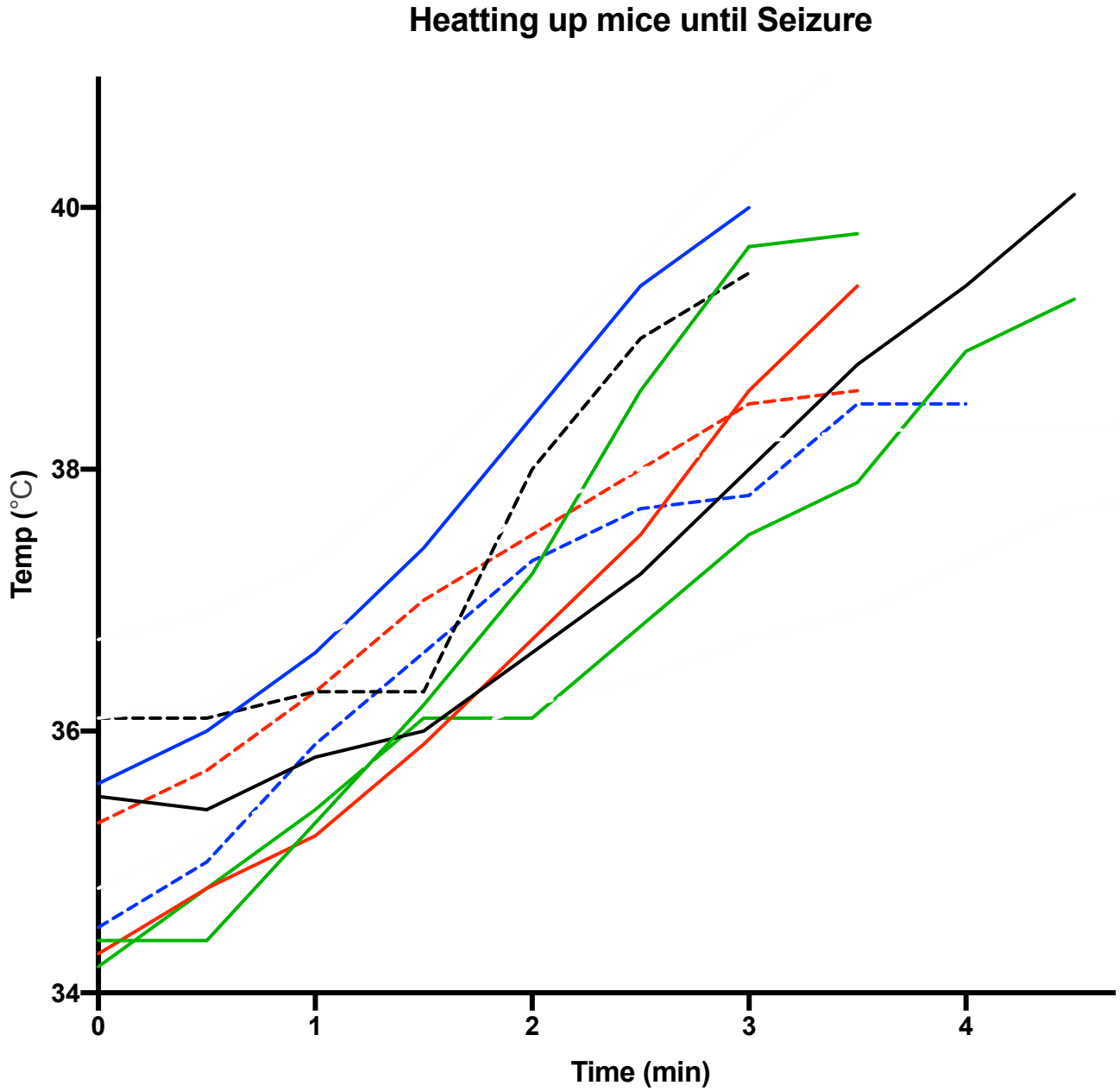
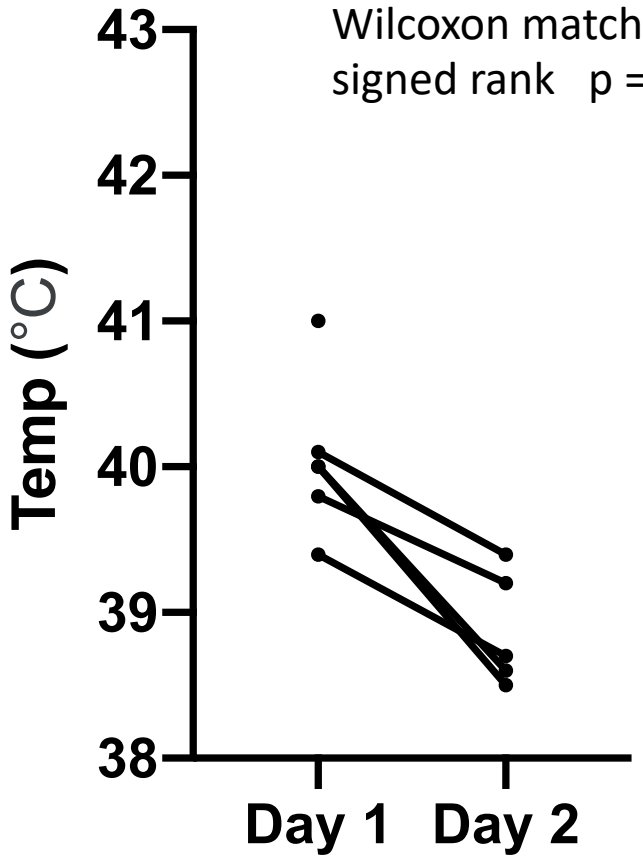


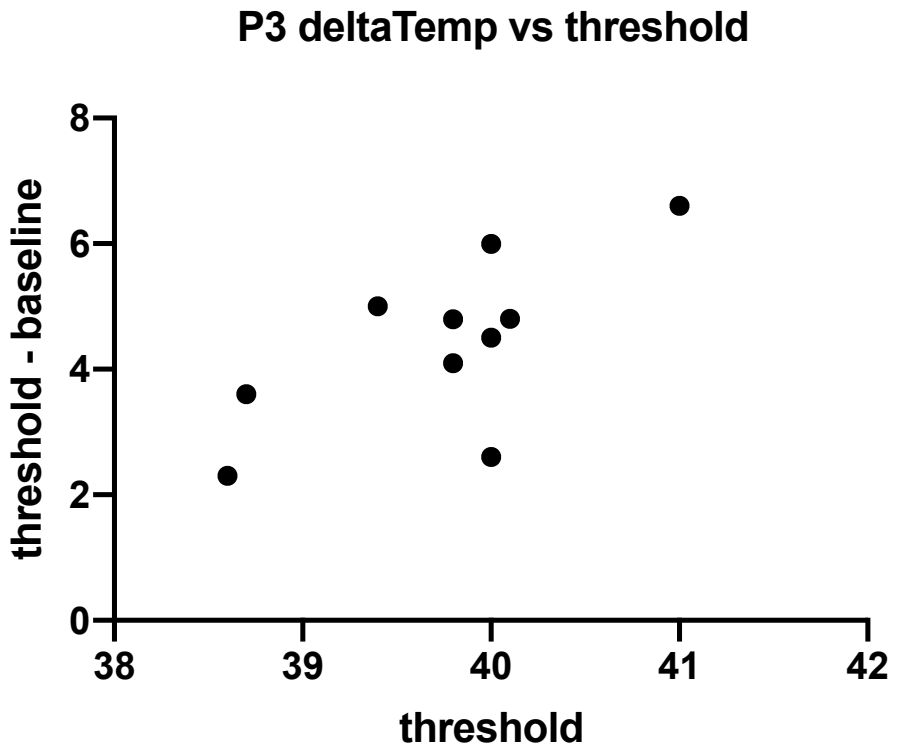
Paired temperature threshold for each animal



33 34 35
base

Do mice have a heat-induced seizure due to the absolute temperature, or due to the amount of heat transferred to them?

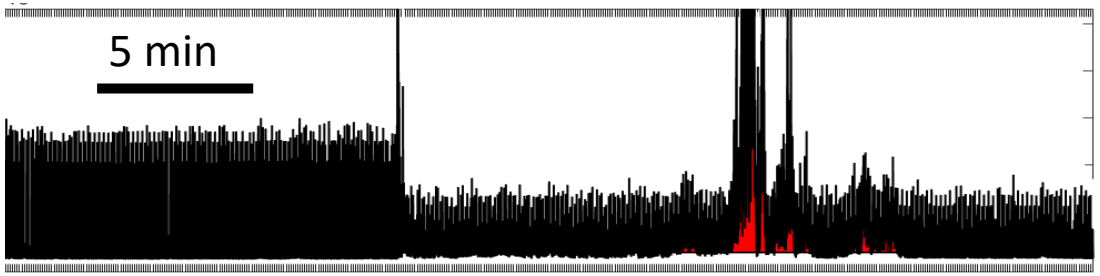
$$Q = k\Delta T = k(T2 - T1) = k(T\_threshold - T\_baseline)$$



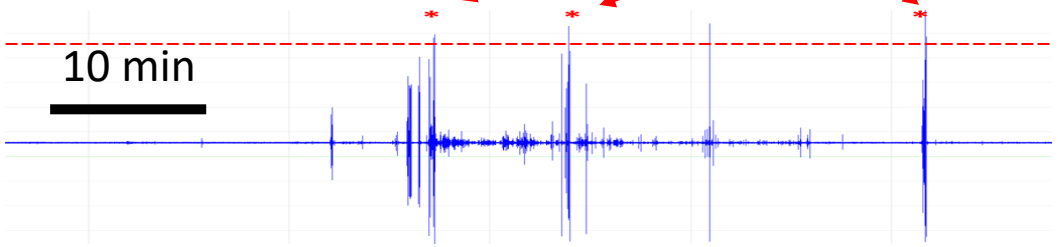
This week: first spontaneous seizure data from Goldberg Lab

DVR recording of group-housed animals → Automated screening for seizure → Confirm seizure on video

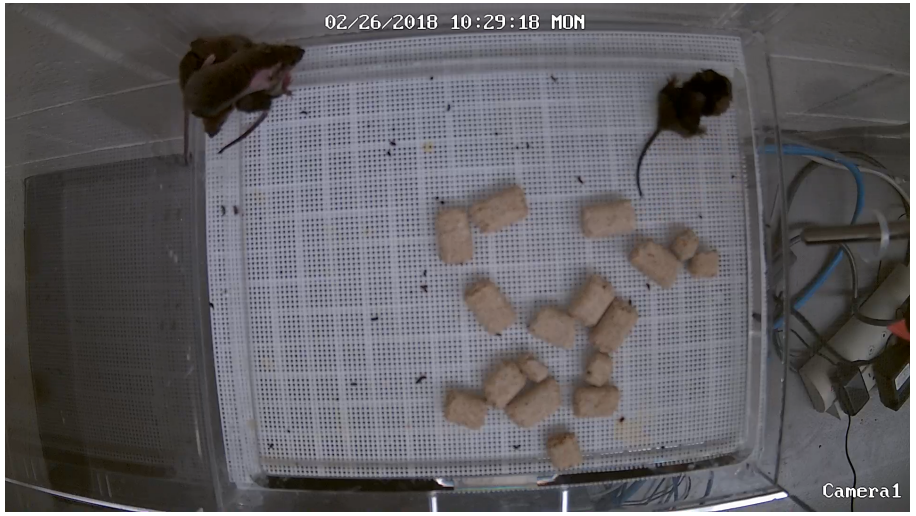
Video screening



Audio screening



confirmed seizures



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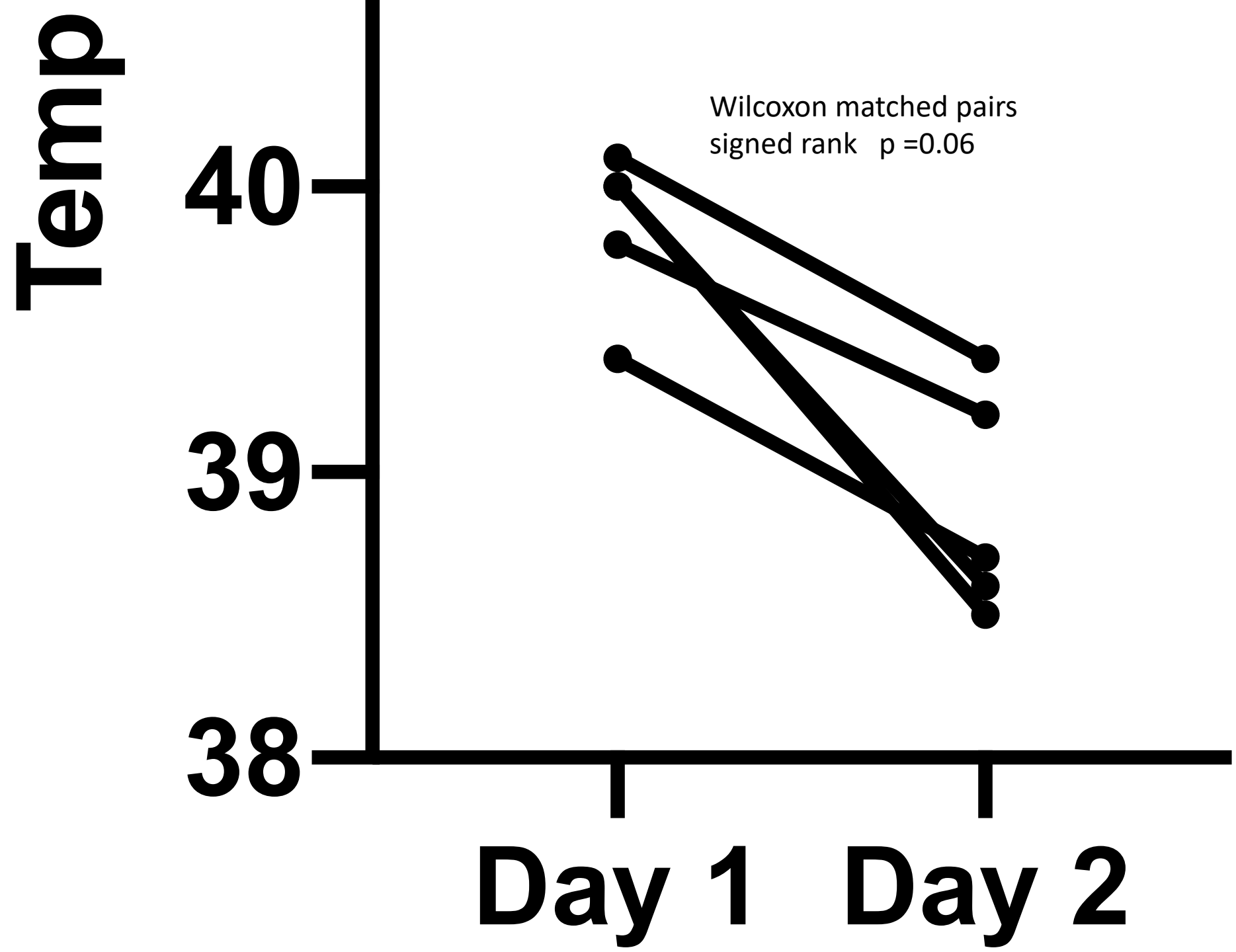
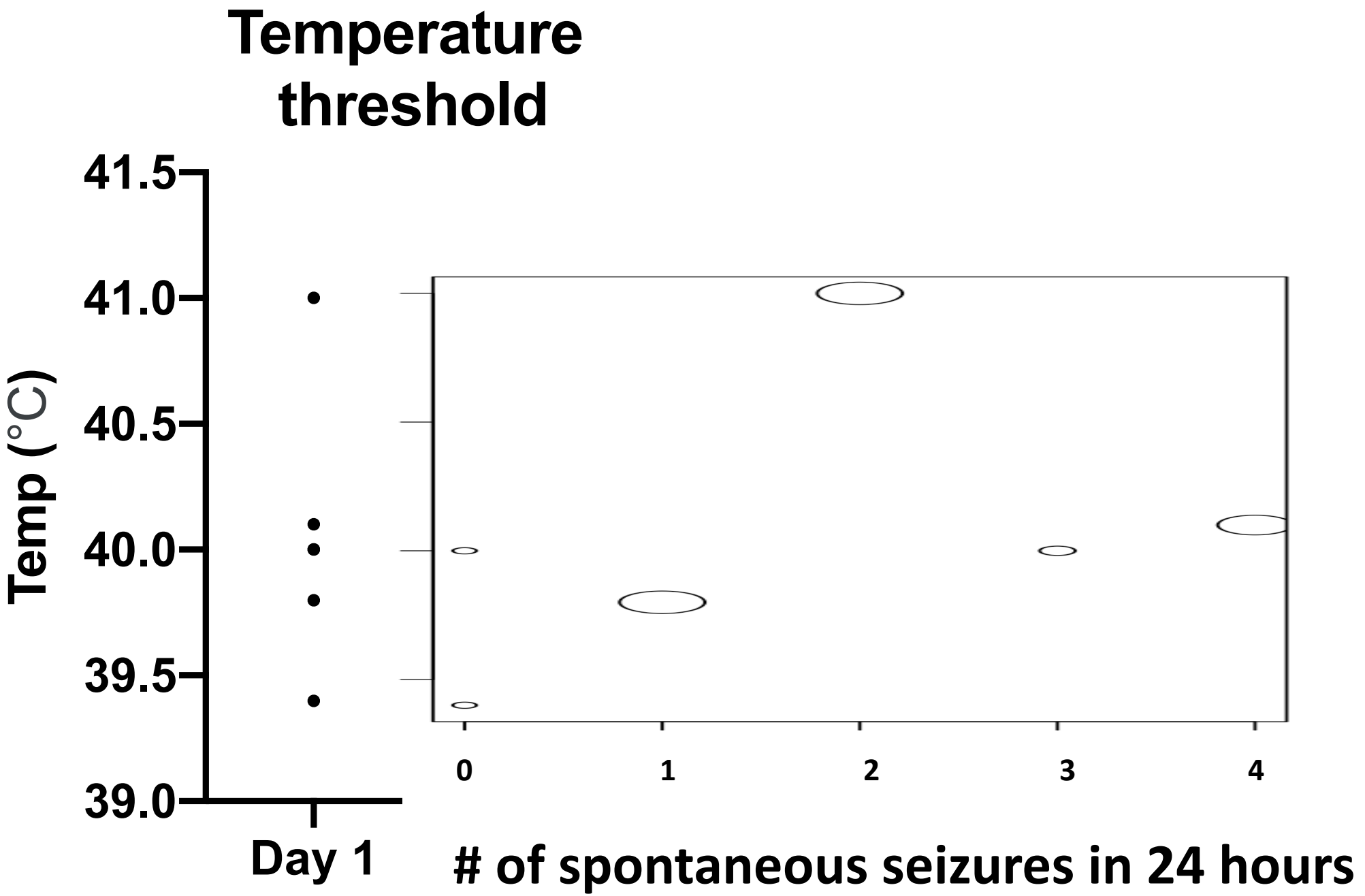
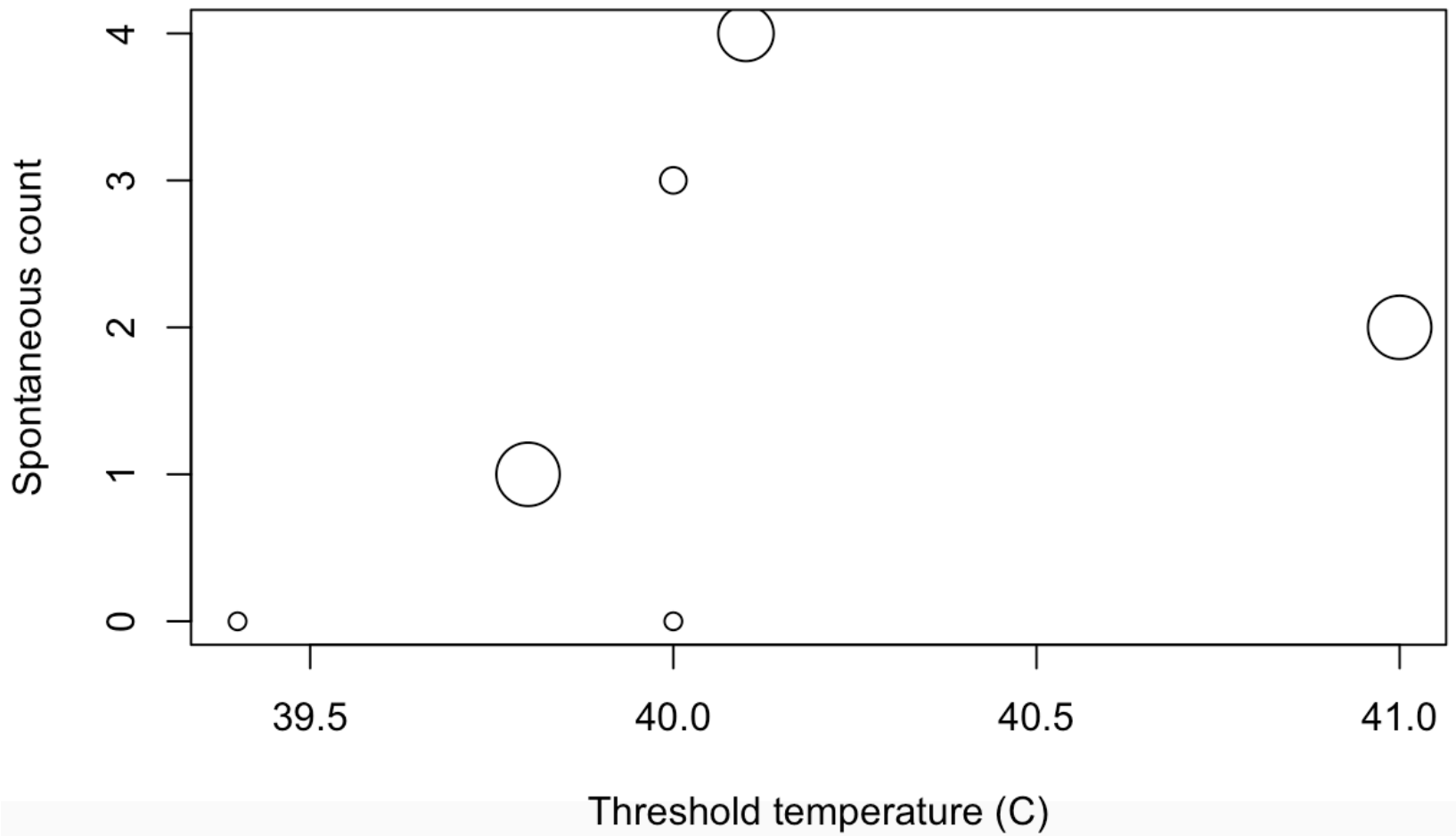

Temp
40
39
38
Wilcoxon matched pairs
signed rank p =0.06
Day 1
Day 2


Temperature threshold
41.5
41.0
40.5
40.0
39.5
39.0
Temp (°C)
Day 1
0
1
2
3
4
# of spontaneous seizures in 24 hours

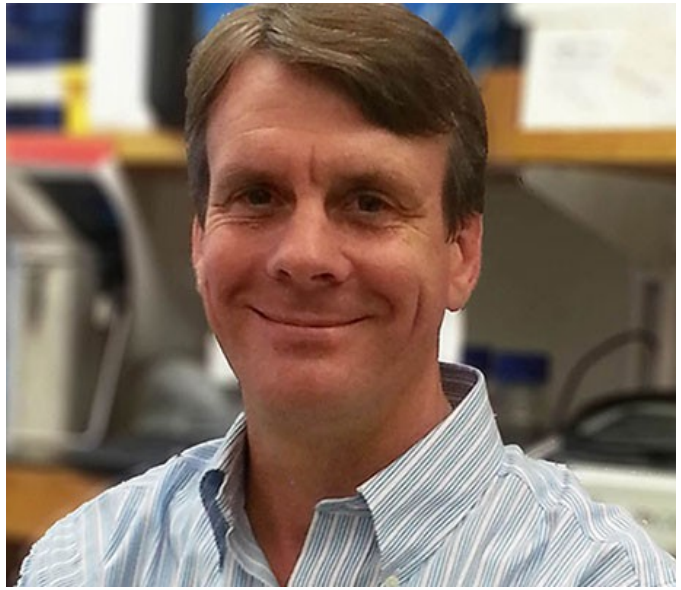
Spearman’s rank correlation test
rho = 0.632, p-value = 0.1779



Acknowledgements

Goldberg Lab

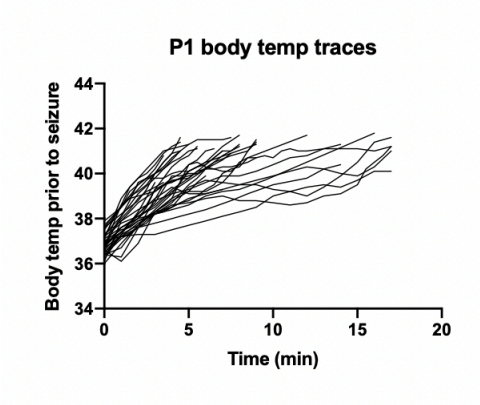
Anderson Lab

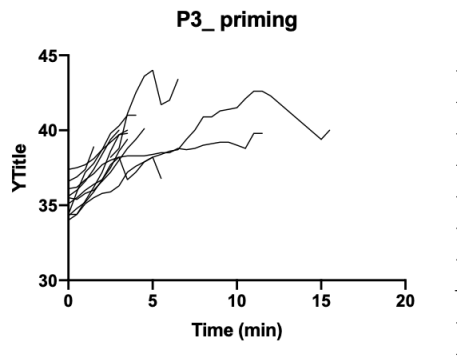


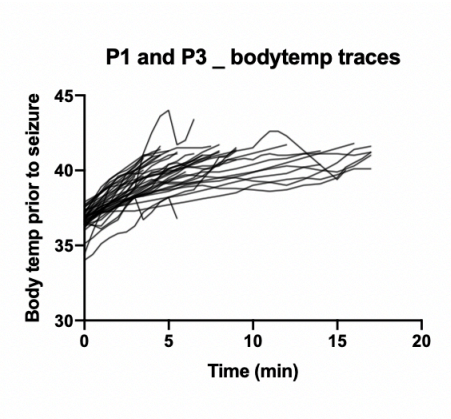
Everyone, especially:

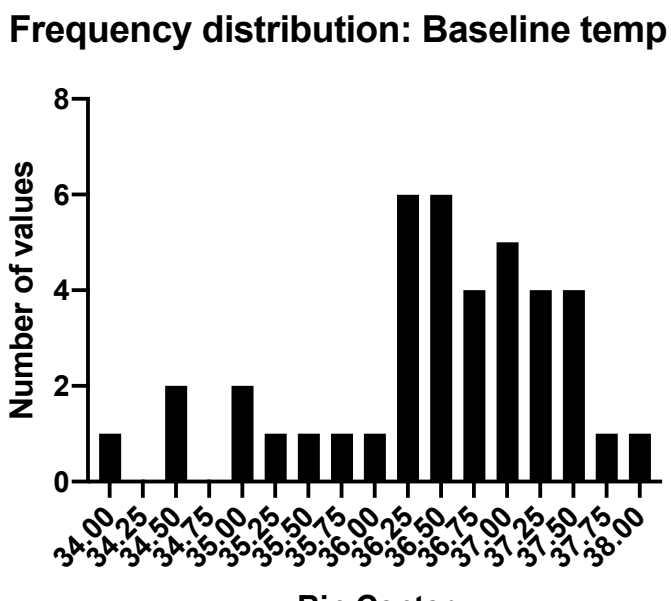
- Madeleine Salvatore
- Xiaohong Zhang, PhD
- Joanna Mattis, MD PhD
- Tariq Zaman, DVM PhD
- Morgana Favero, MD
- Sean Ryan
- Kevin Goff
- Aliza Ohnouna
- Jina Yom
- Shane Fitzgerald

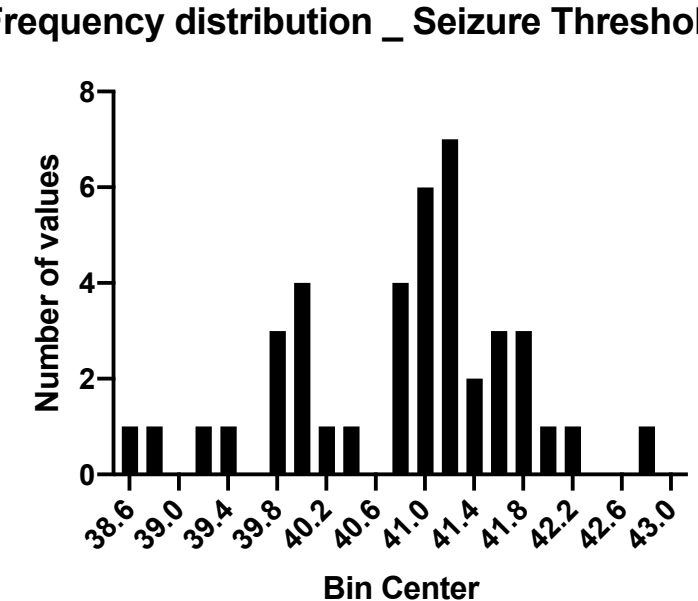
Heat-induced seizure protocol

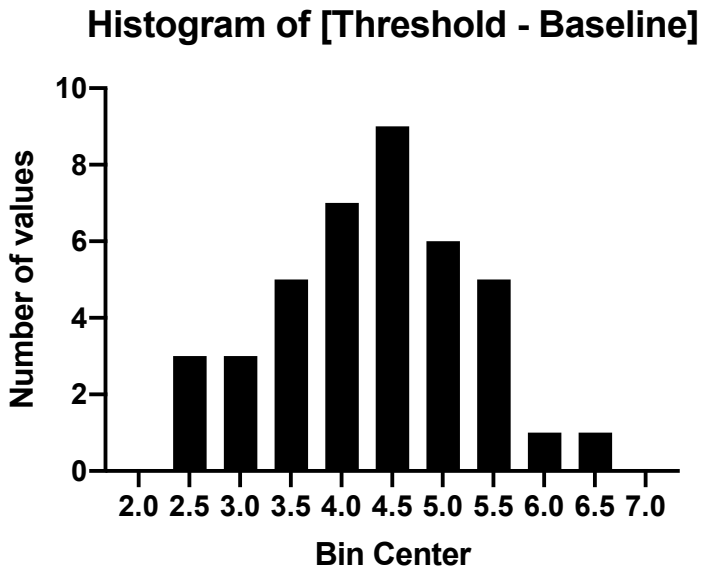




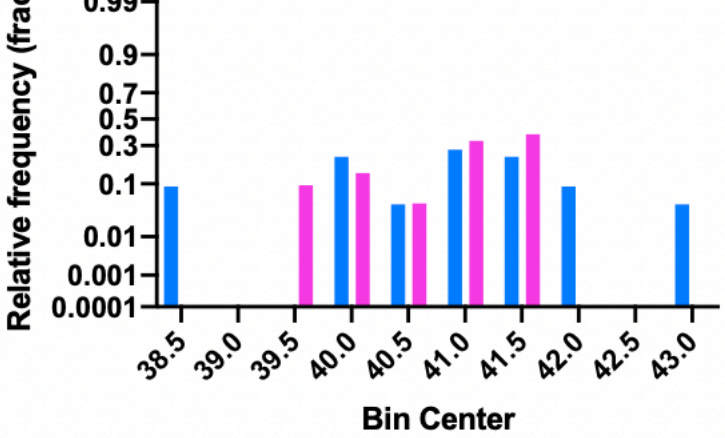


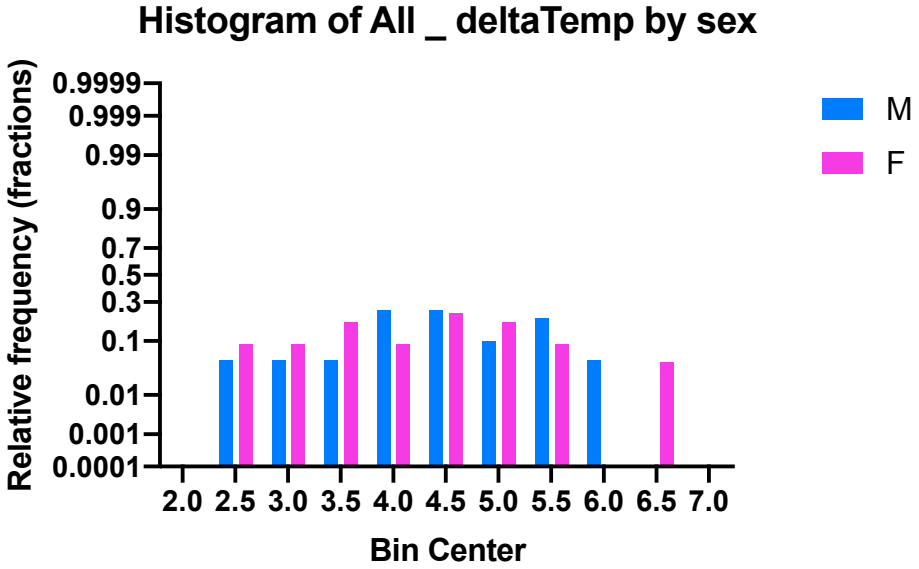


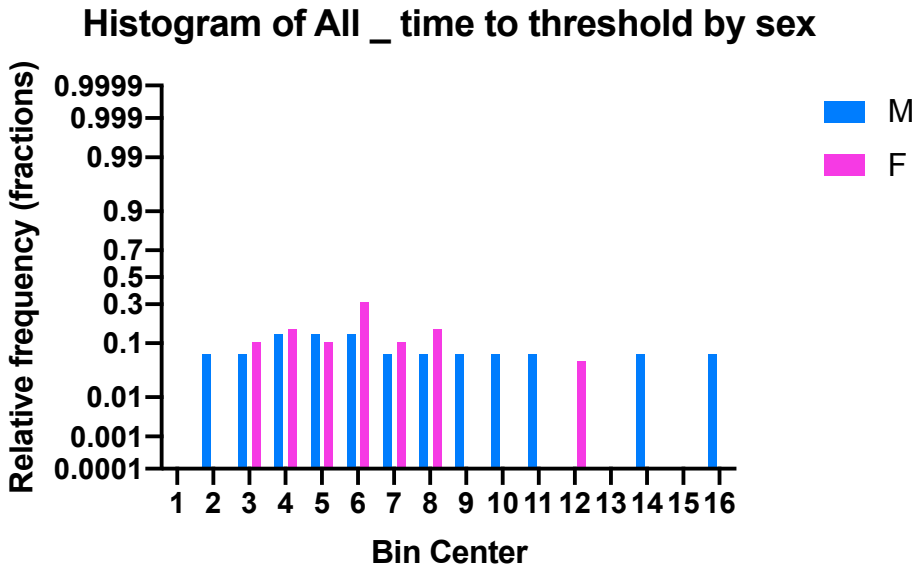




Looking at each me



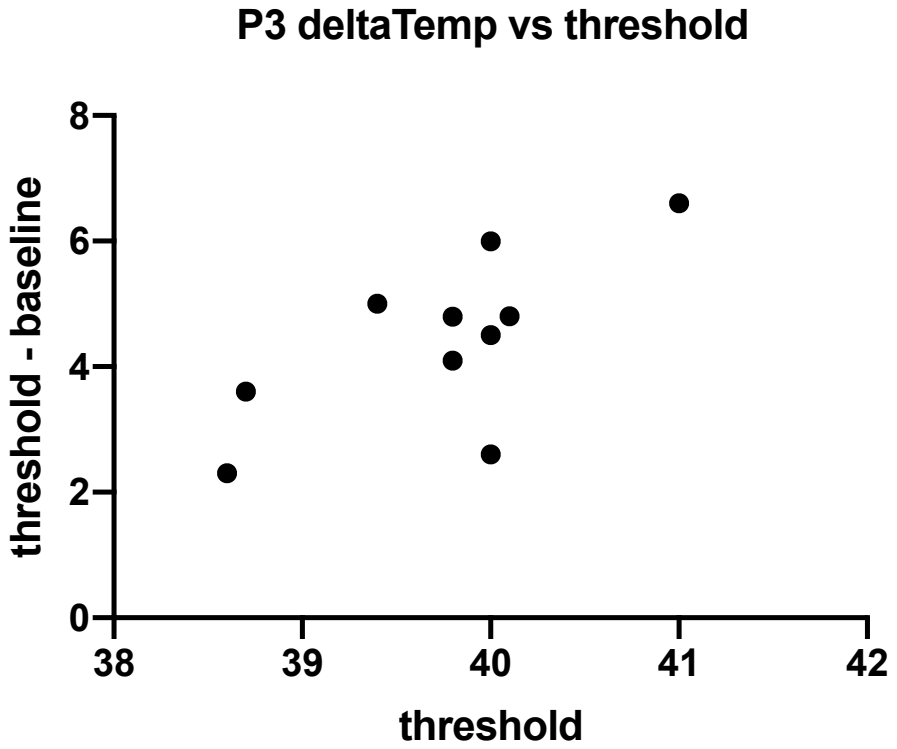




33 34 35
base

Does baseline correlate with threshold?

Change in temp



Time to seizure