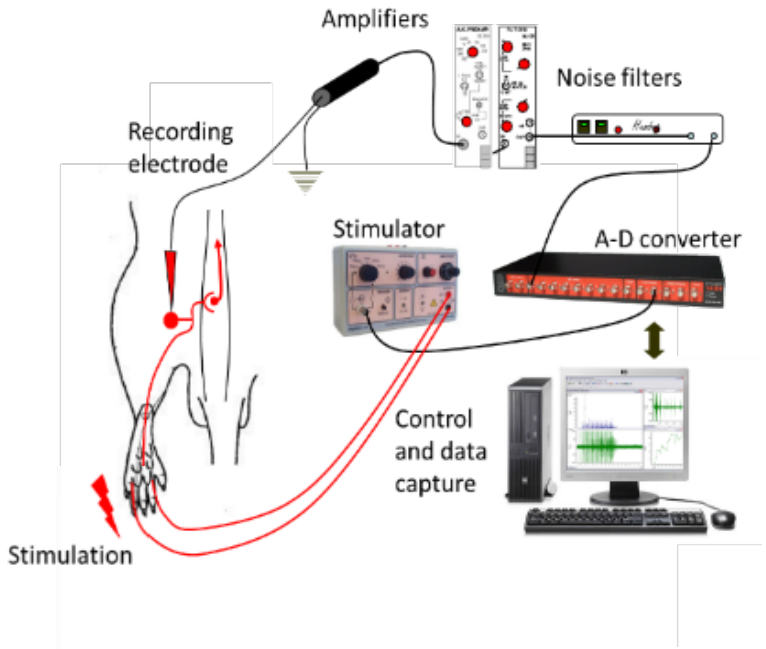
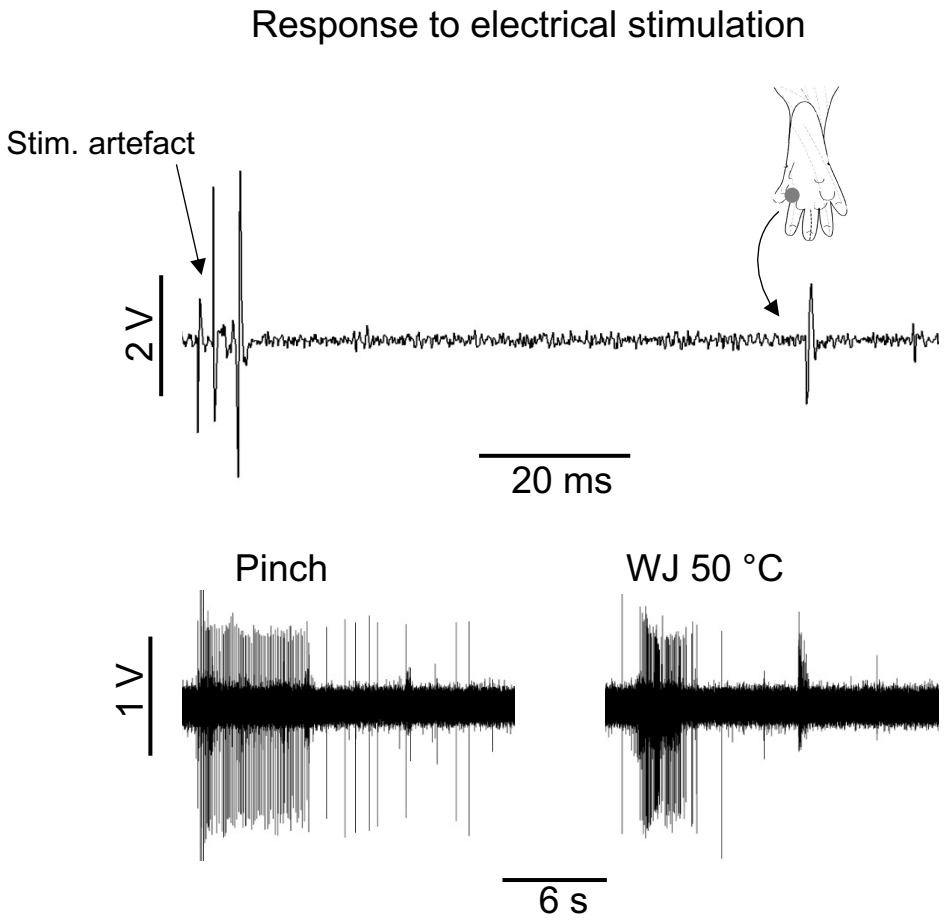
In vivo recordings of DRG neurons

neuroservices ALLIANCE

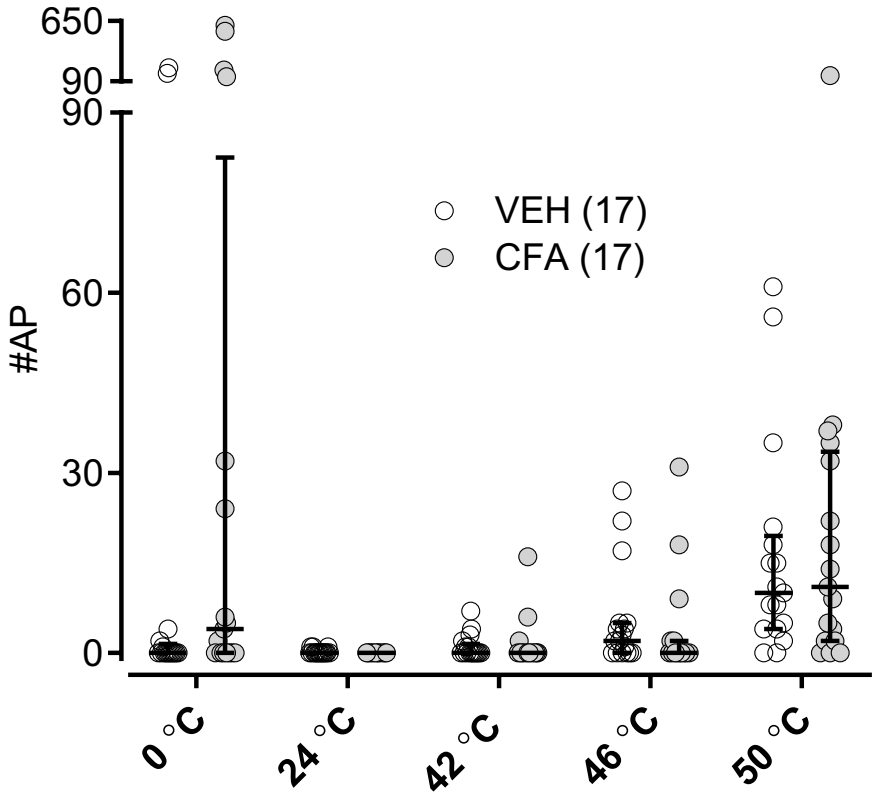
Recording of DRG neurons

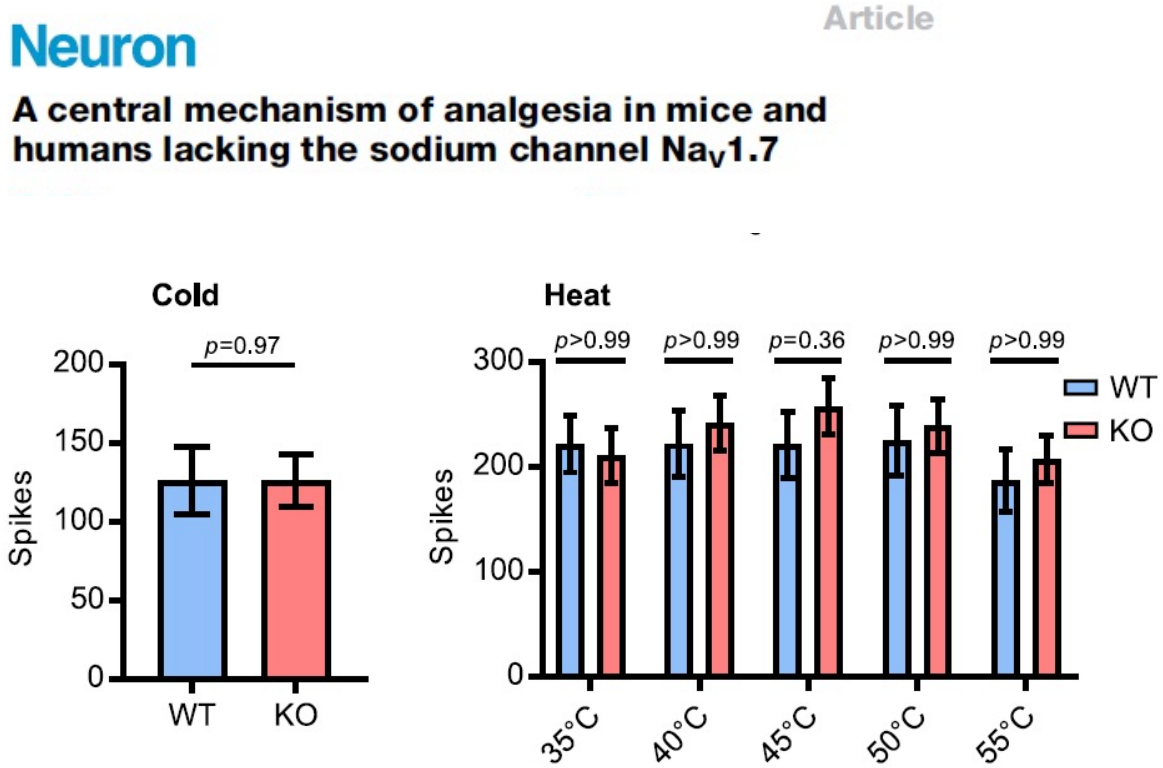




- The essential challenge is to obtain a sufficient signal-to-noise ratio when recording from unmyelinated nociceptor.

Don't get them mixed up…





- Left hand side: in house data (previous study).
- Right hand side: published data using the same technique (https://doi.org/10.1016/j.neuron.2021.03.012).

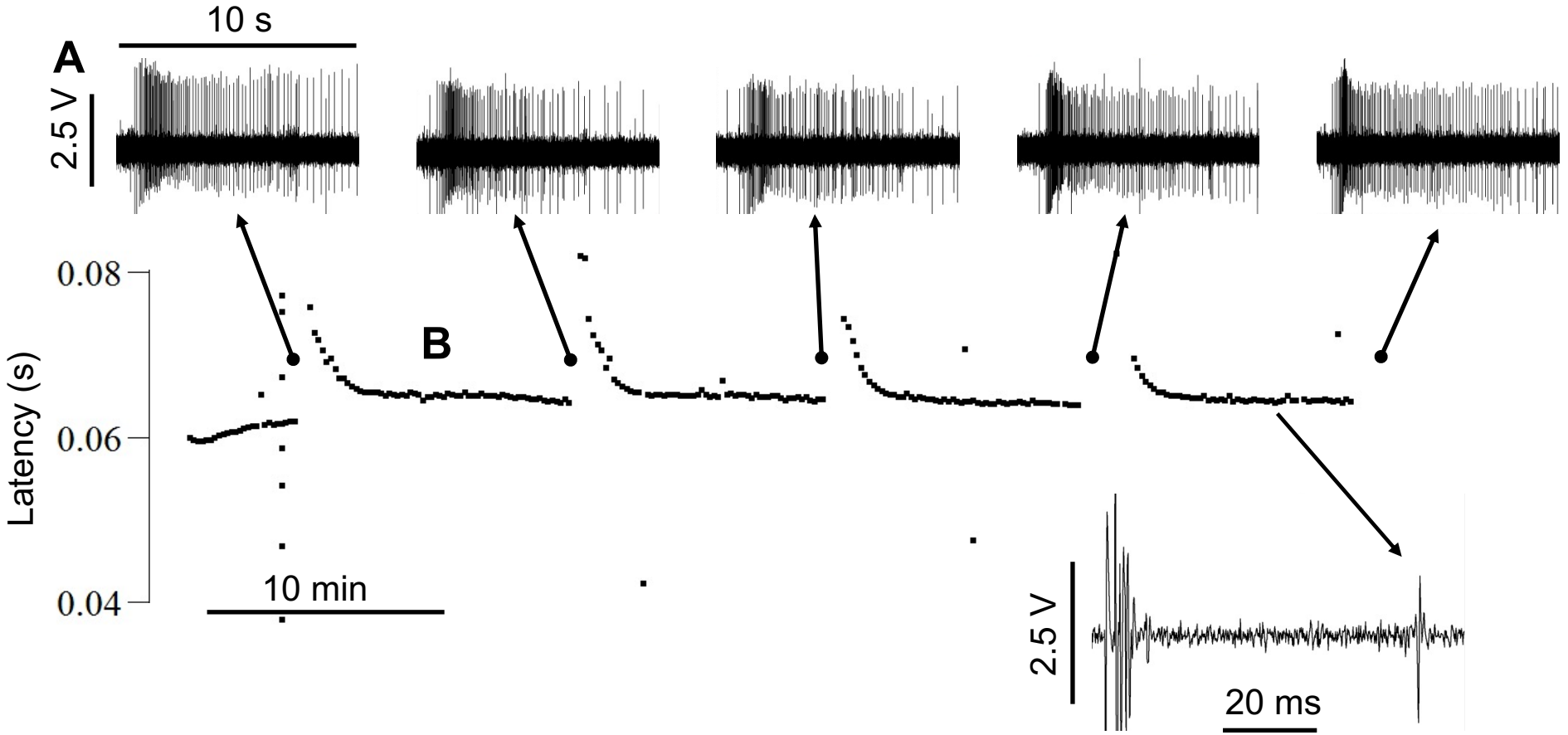
About assessing the efficacy of Nav1.7 channel blocker in vivo on electrophysiological endpoint

Nav1.7 is a challenging target prone to generate false positive:

- IC50 derived from in vitro experiments is highly dependent on specific testing conditions (voltage, etc…), leading to mismatch between in vitro IC50 and actual in vivo IC50.
- The development of highly hydrophobic structure may lead to “true” Nav1.7 channel blocker with excessive protein binding fraction (Pfizer compound?).
- Lack of in vivo selectivity results in Nav1.6 channel blockade which might lead to apparent efficacy in behavioural test.

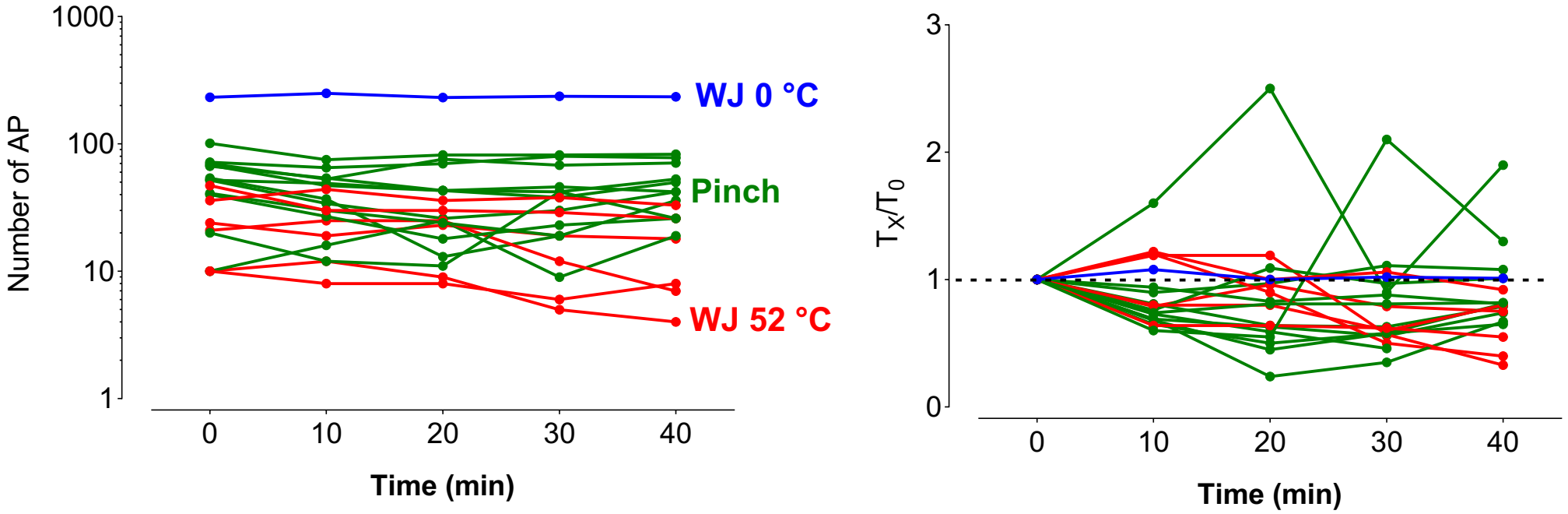
neuroservices ALLIANCE

Combining natural and electrical stimulations



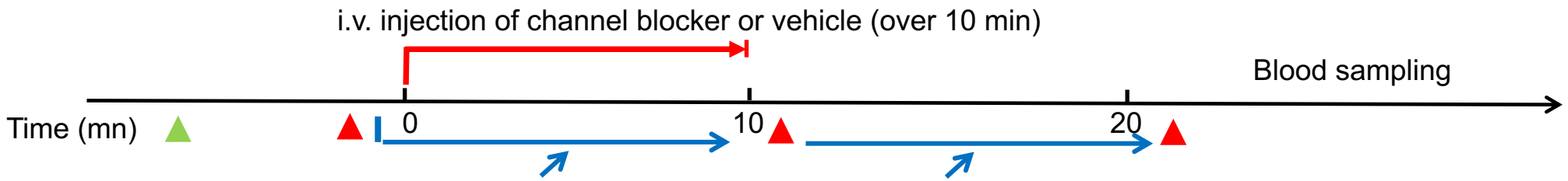
- All illustrations are extracted from one recording. Pinch was applied 5 times every 10 min (A), and electrical stimulations were applied in between to obtain a raster plot of the latency of the action potential (analogue view in C).

Desensitization might occur for some DRG neurons



- Quantification of responses in 20 experiments following the protocol illustrated on the previous slide (23 mice were experimented). There was a run down of the response for some neurons.

Protocol for assessing Nav1.7 channel blocker



▲ : response to mechanical and thermal stimuli
- brush, VF25, 50, 100, 200 mN and pinch
- Water Jet (10 ml): 0, 24, 44, 48 and 52 °C

▲ : pinch or 0 °C or 52 °C

↗ : peripheral electrical stimulation
- 1 pulse every 10 s

Variables:
- Strain of mice (Swiss)
- Status: control
- Stimulus modalities: ad hoc noxious mechanical or thermal + noxious electrical
- Sampling: blood (+ sciatic nerve?)
- Compound: dose and formulation

Contact us

Raymond Price, PhD, EMBA
Chief Business Officer
Raymond.price@neuroservices-alliance.com
Mobile - +1 (858) 649 9403

Julien Allard, PhD
CSO,
In Vivo Spinal Cord & DRG Electrophysiology
julien.allard@neuroservices-alliance.com
Mobile - +33 (0) 6 45 07 13 16

neuroservices ALLIANCE

The CNS Electrophysiology CRO

WWW.NEUROSERVICES-ALLIANCE.COM