



Multisine Frequency Modulation of Intra-epidermal Electric Pulse Sequences to Study Nociceptive Processing: Methods and Limitations

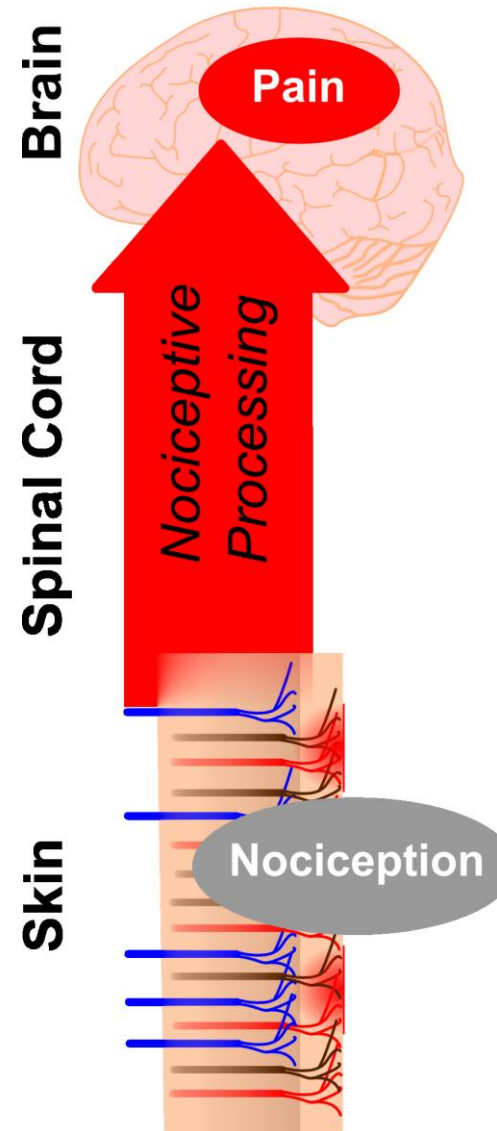
Boudewijn van den Berg*, Mana Manoochehri, Mindy Kasting,
Alfred C. Schouten, Frans C.T. van der Helm, Jan R. Buitenweg

**UNIVERSITY
OF TWENTE.**

**TU Delft**

Introduction

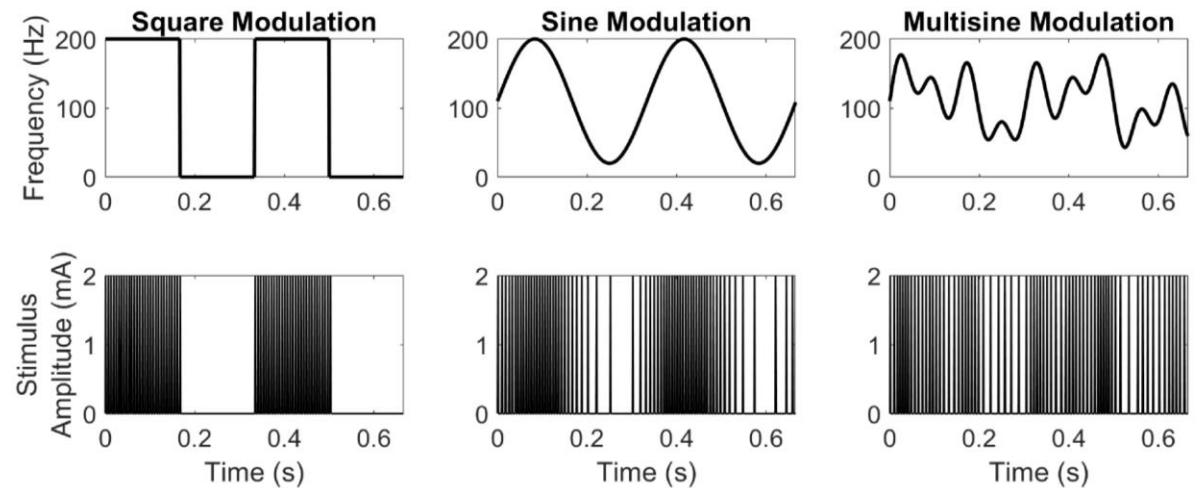
- Unclear how pain is generated by nociceptive input.
- Relation between nociceptive and brain activity.
- Evoked potentials reflect stimulus salience:
 - Not stimulus modality (i.e. tactile vs. nociceptive)
 - Short stimulus
- Steady-state evoked potentials (SSEPs) reduce effect of salience.
- SSEPs are more similar to tonic pain.





Why nociceptive multisine SSEPs?

- Recent studies demonstrate nociceptive SSEPs (laser, thermode).
- Square modulation:
 - activates harmonics
 - does not generate a continuous sensation
- Multisine modulation can be used to assess:
 - (non)linearity
 - system order
 - system delay
 - signal-to-noise ratio





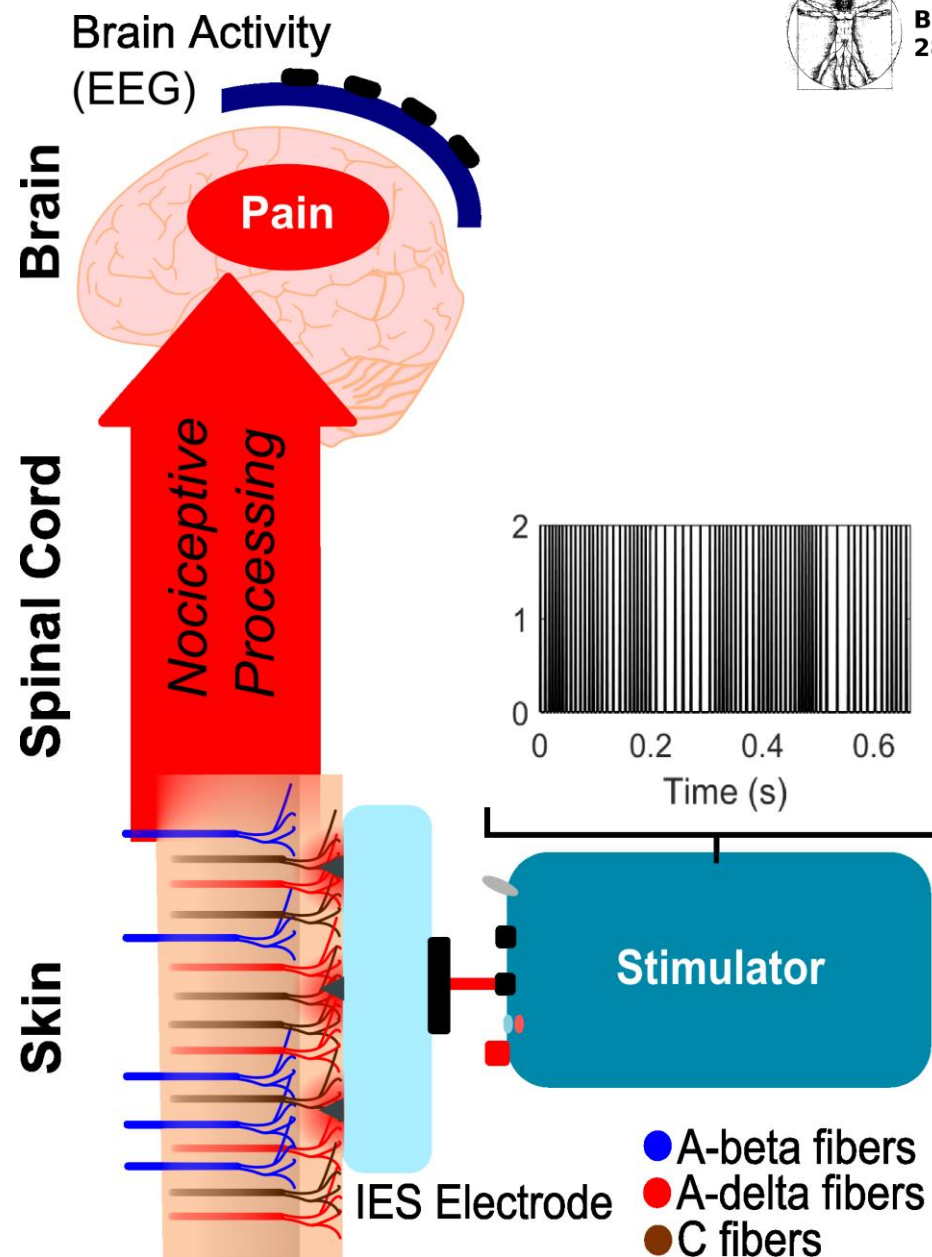
Why this presentation?

- Second study to measure nociceptive SSEPs using electric stimulation.
- First study to measure nociceptive SSEPs through (multi)sine stimulation.
- Method and limitations (i.e. problems!)



Method

- Intra-epidermal electric stimulation.
- Activation of nociceptive afferents.
- Multisine modulation of pulse sequence at 3, 7 and 13 Hz.
- Bandwidth of 20 to 200 Hz.
- 100 sequences per experiment.
- Proof-of-principle on 10 subjects.



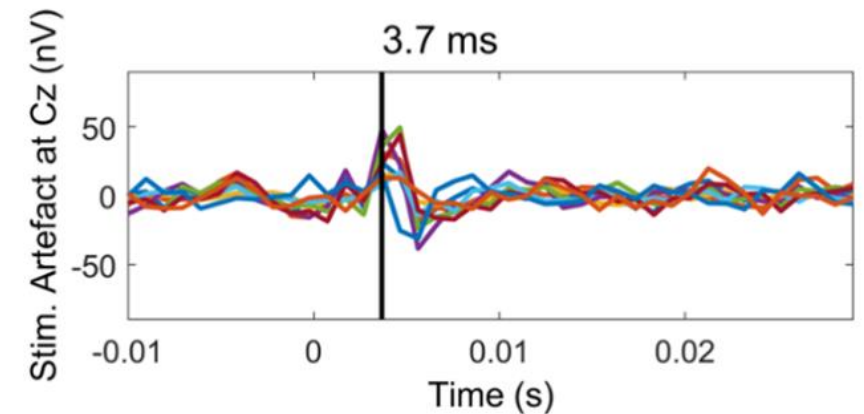
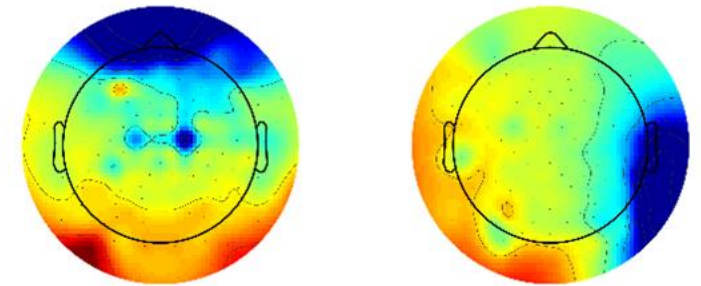


Problem 1: Stimulation Artefact

- Volume conduction current
- Displacement current
- Electromagnetic coupling

1. Do not trigger every pulse!
2. Scrub, scrub more, and use gel.
3. Choose proper ground locations.

Forehead Ground Mastoid Ground

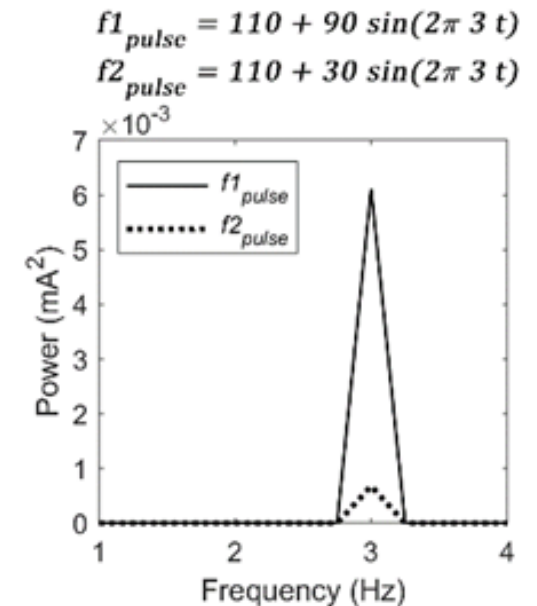
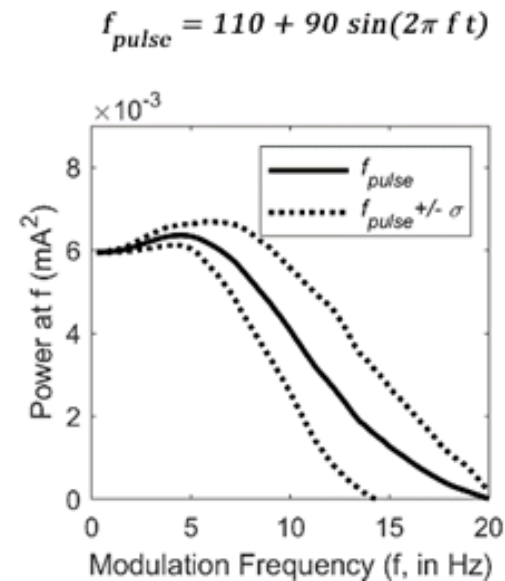




Problem 2: Limited Bandwidth

- Available bandwidth ± 20 to 200 Hz.
- Power decrease as modulation frequency approaches pulse frequency.
- Power decrease by sharing bandwidth.

1. Optimize bandwidth usage with opposite phases (e.g. $-\pi/2$, 0 , $\pi/2$)





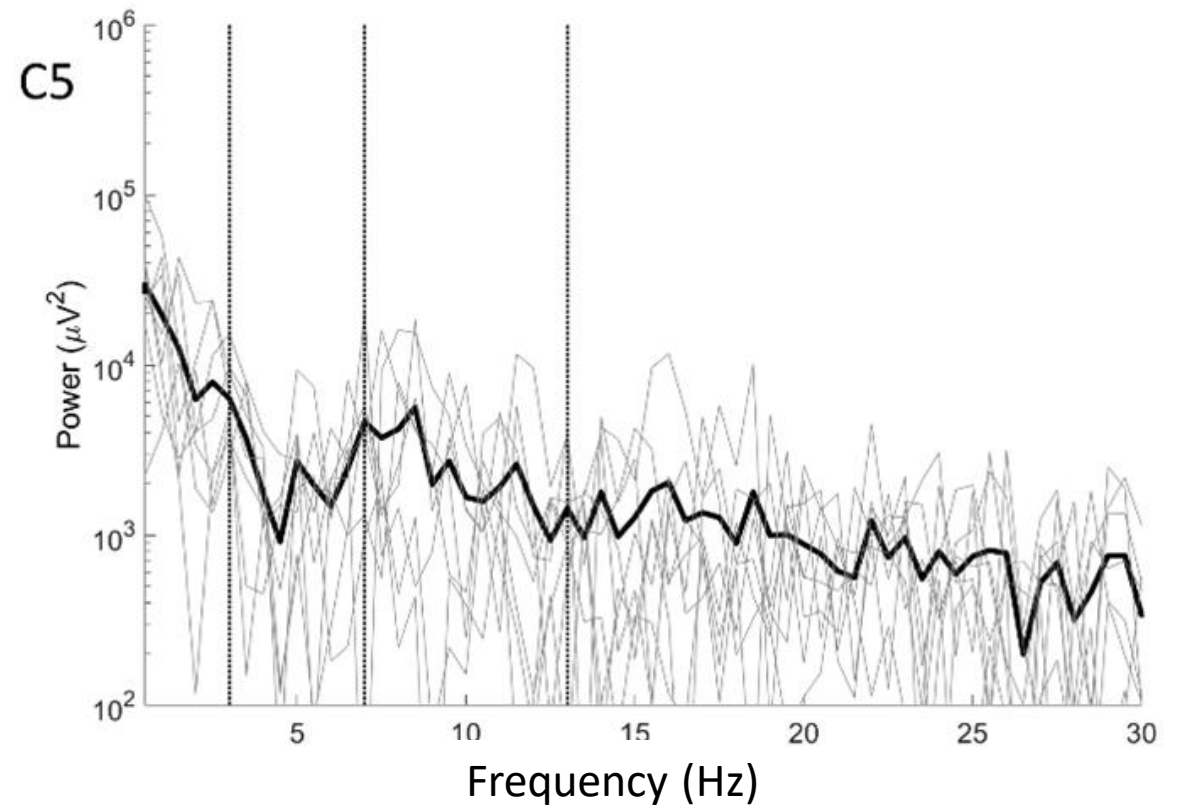
Problem 3: Physiological Noise

- Movement and EOG (\pm 0-3 Hz)
- Alpha Waves (\pm 8-12 Hz)
- Muscle Activity (\pm >20 Hz)

1. Sufficient rest is essential.

2. Use advanced filtering techniques (e.g. AMICA).

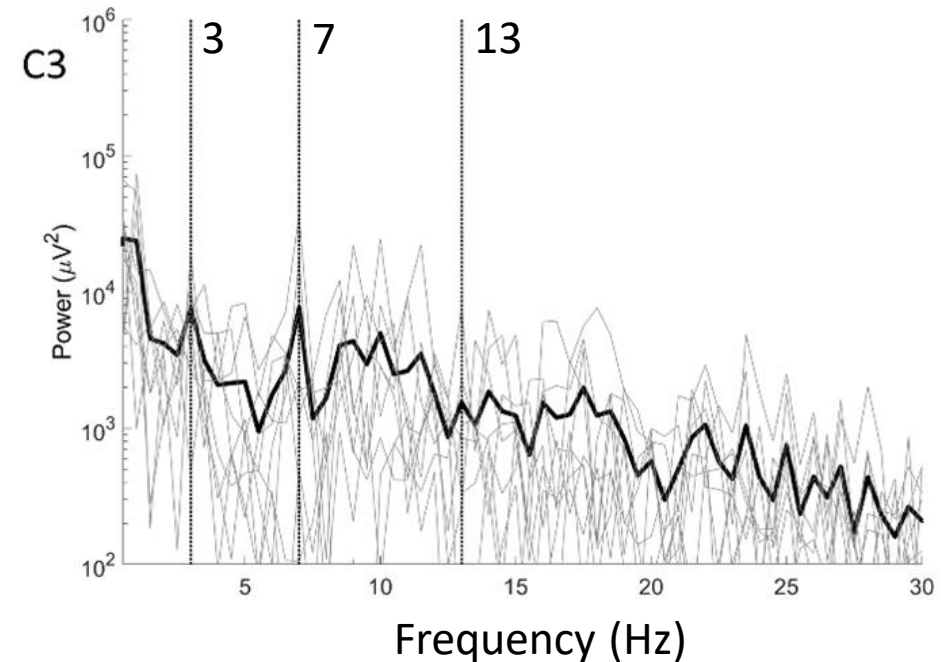
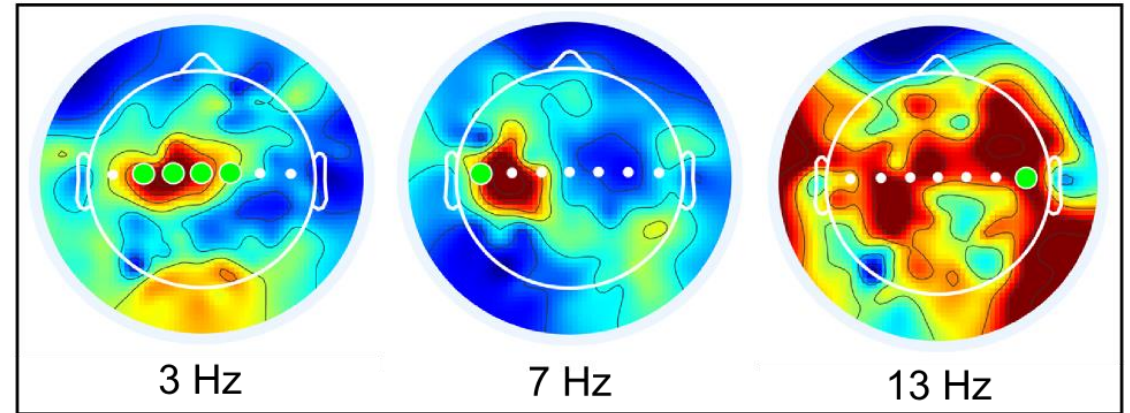
2. Avoid overlap with physiological frequencies!





Preliminary Results

- Clear SSEP at 3 and 7 Hz.
- No harmonic activity.





Discussion

- Multisine modulated intra-epidermal stimulation evokes brain activity at fundamental frequencies.
- Improve signal-to-noise ratio while reducing stimulation artefact:
 - Minimize impedances.
 - Optimize bandwidth usage.
 - Minimize physiological artifacts.

Current challenges:

- Habituation
- Modulation of brain oscillations
- Source localization



Questions?

E-mail: b.van.den.berg@utwente.nl

Researchgate:

https://www.researchgate.net/profile/Boudewijn_Van_Den_Berg2

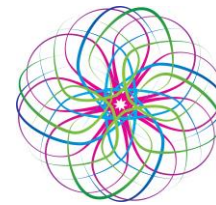
Soon to be published:

Multisine Frequency Modulation of Intra-epidermal Electric Pulse Sequences: A Novel Tool to Study Nociceptive Processing

UNIVERSITY
OF TWENTE.

 TU Delft

 TIMSi



CHDR
Centre for Human Drug Research



NeuroControl

 NociTRACK

 NWO | Applied and
Engineering Sciences

NeuroCIMT: Project NOCICEPT

<http://neurocontrol.nl/neurocimt-project-2-nocicept/>