Continuous Pain Intensity Estimation from Autonomic Signals with Recurrent Neural Networks

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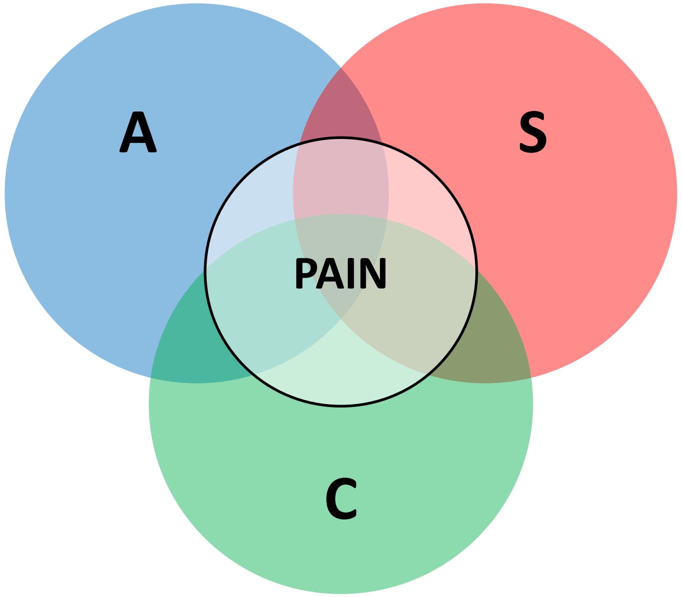
What is pain?

"Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive and social components."

A. C. de C Williams and K. D. Craig. Updating the definition of pain. Pain, 2016

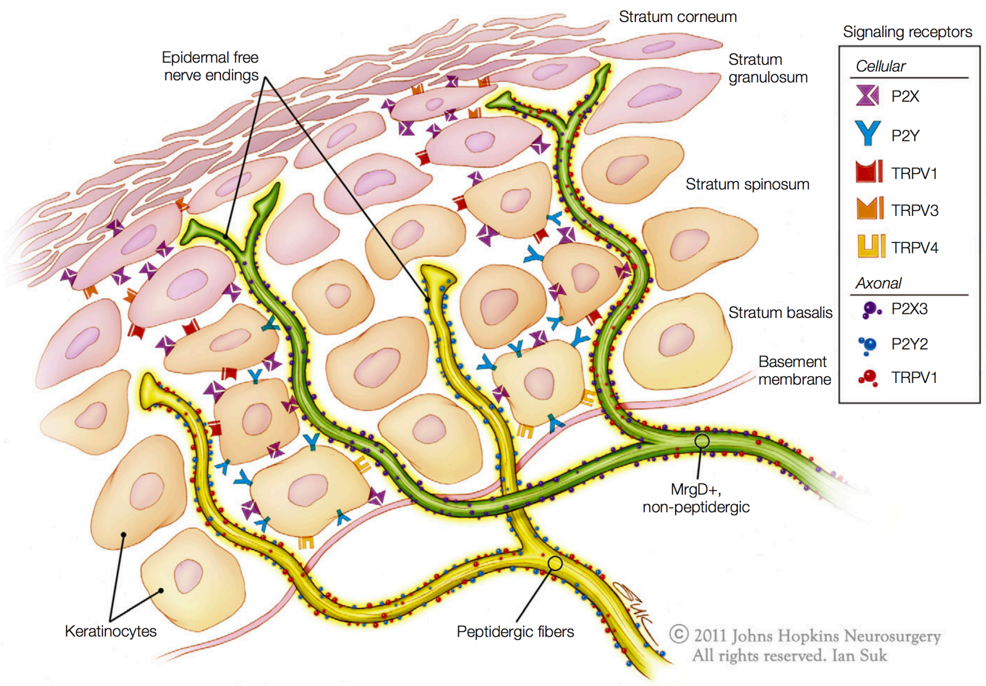
Affective: Negative emotion: anxiety, fear, unpleasant sensation.

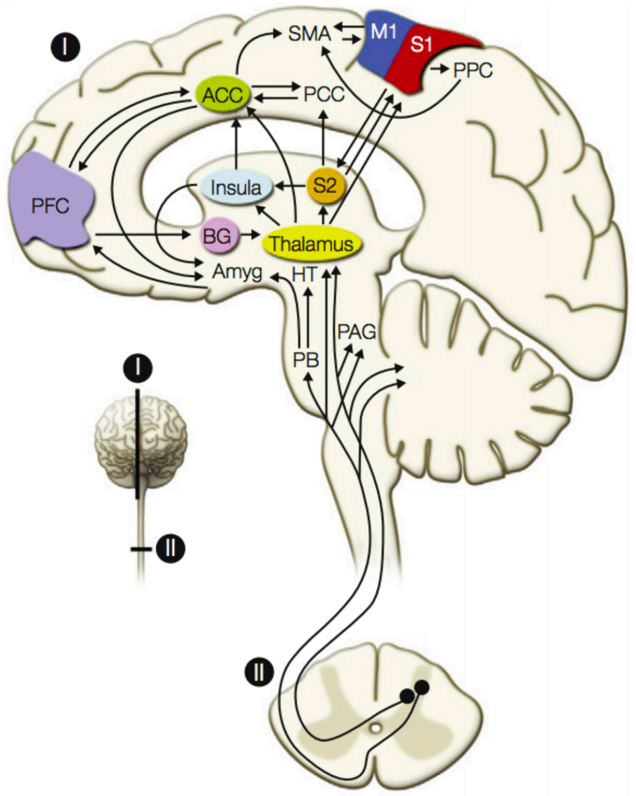


Sensory: Perception of pain characteristics: intensity, quality, location.

Cognitive: Interpretation of pain.

Pain ≠ nociception

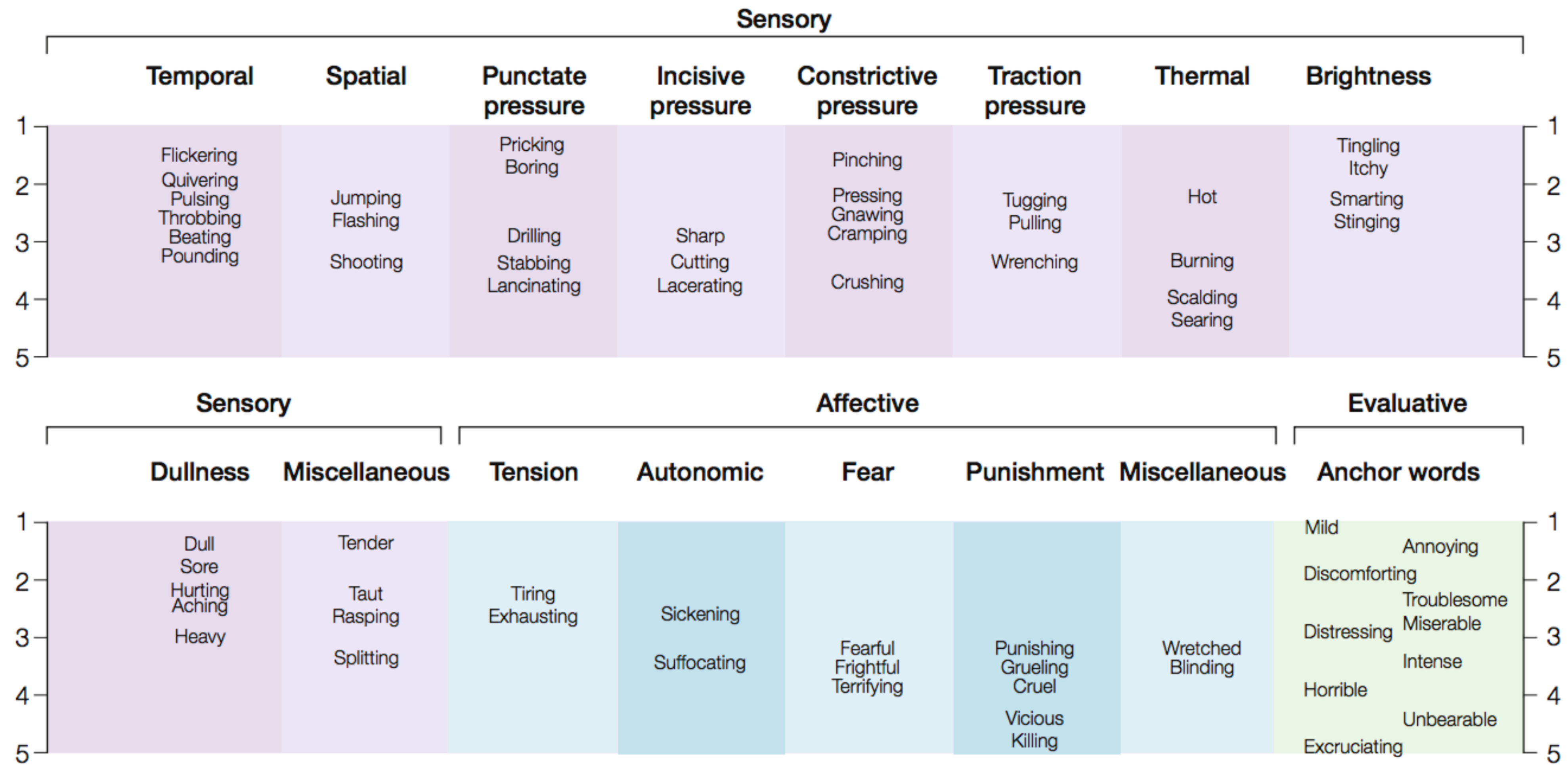




- **Nociception** refers to the peripheral and central nervous systems processing information generated by stimulation of nociceptors by noxious stimuli.
- Nociception can occur in the absence of pain.
- **Pain** is a product of higher brain center processing of signals it has received.
- Pain can occur in the absence of nociception (e.g. neurogenic pain).

Figures reproduced from: Wall & Melzack's Textbook of Pain, Sixth Edition

Self-report: the gold standard of pain measurement



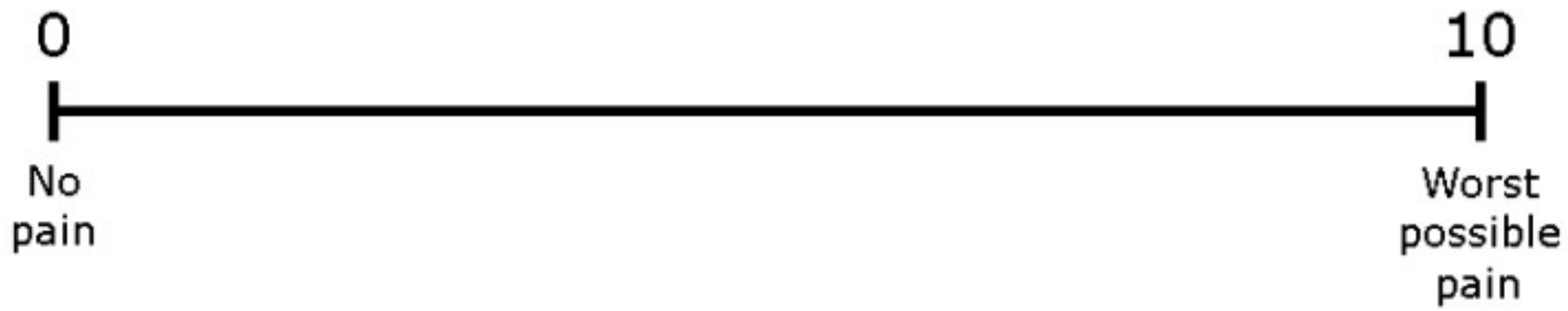
Pain descriptors based on intensity ratings by patients

Wall & Melzack's Textbook of Pain, Sixth Edition

Self-report: the gold standard of pain measurement

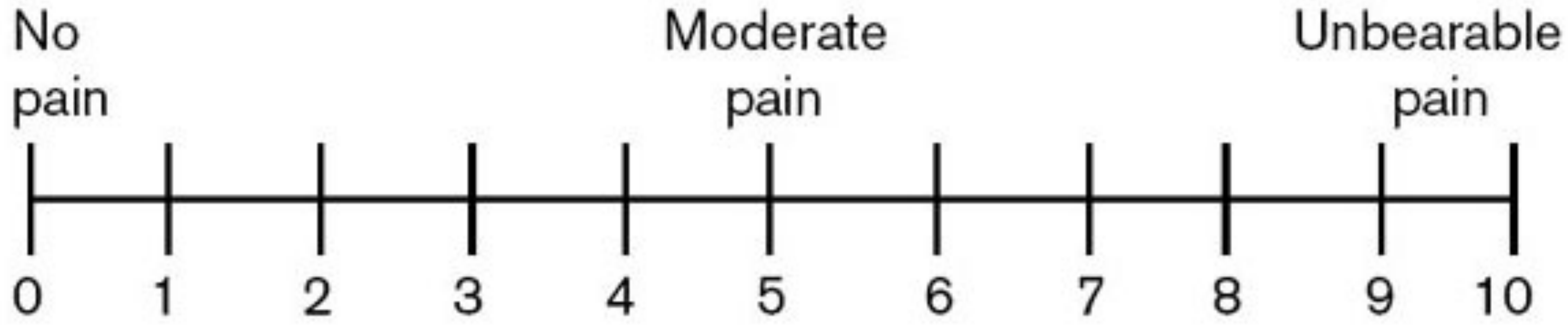
VAS

Visual Analog Scale



NRS

Numerical Rating Scale



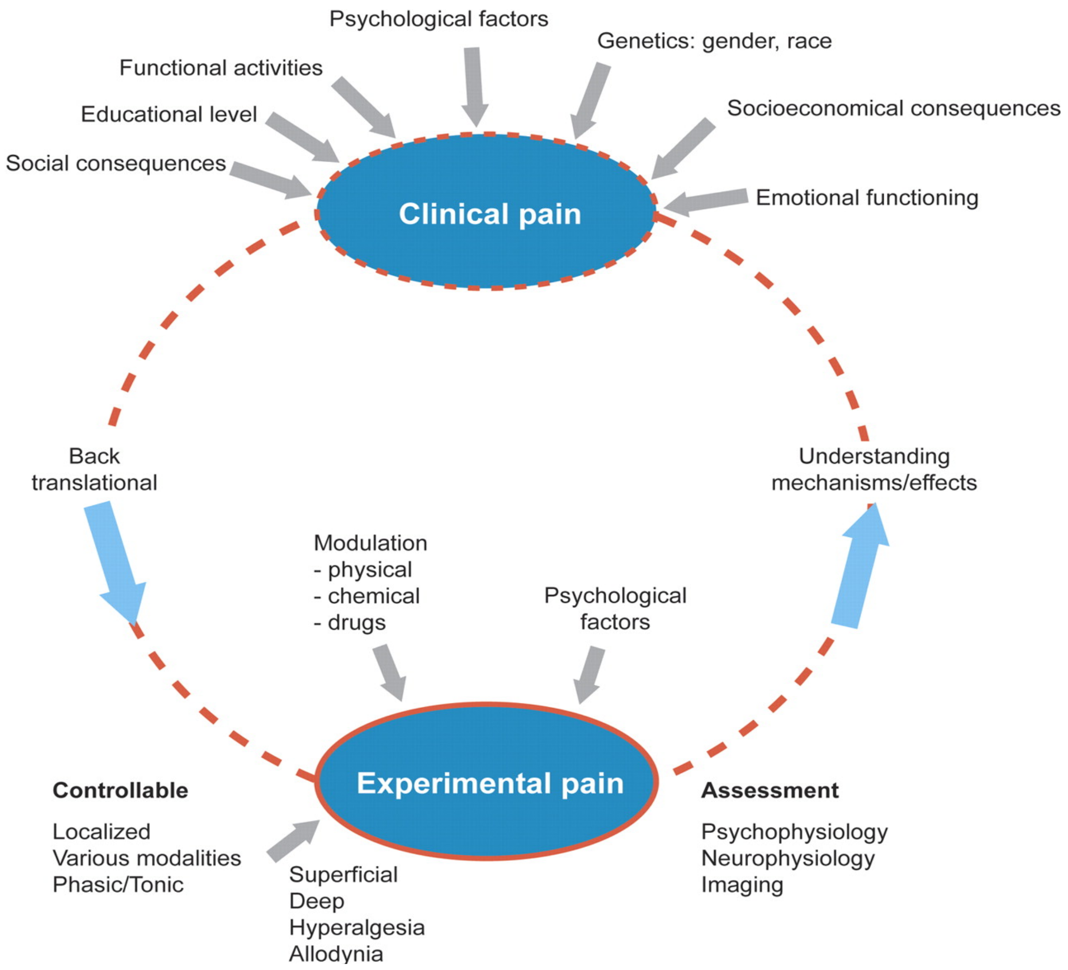
When self-report fails… Automatic Pain Recognition

When pain cannot be communicated

Large-scale clinical studies

Human-robot interactions

Experimental pain elicitation methods and human models of pain



Experimental pain models are important for study of mechanisms which could not be studied in patients but could be standardized and modified for clinical use.

Pain elicitation methods:

- Heat
- Cold
- Electrical
- Chemical
- Mechanical

Pharmacol Rev 64:722–779, 2012

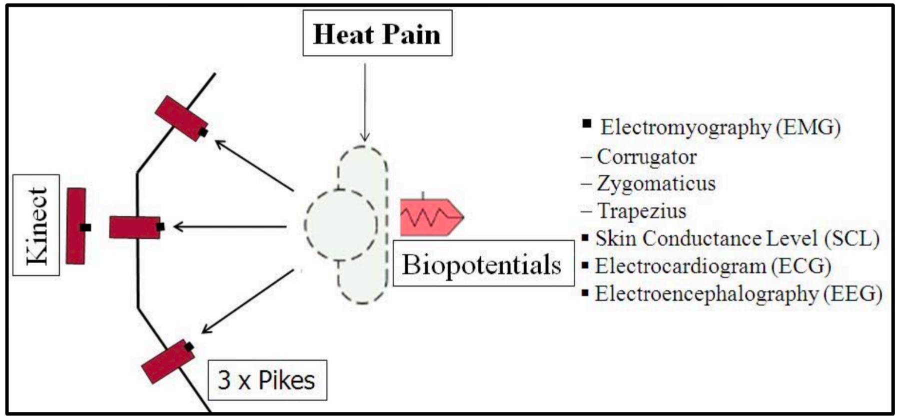
BioVid Heat Pain Database

Pain stimulation
PATHWAY thermode at right arm

Participants
- 90 subjects in three age groups:
  a) 18-35 (N = 30; split half man/women)
  b) 36-50 (N = 30; split half man/women)
  c) 51-65 (N = 30; split half man/women)

Measured biopotentials
- Skin conductance
- EKG (2 electrodes)
- EMG (2 channel, for for corrugator, zygomaticus and trapezius muscles)
- EEG (21 channels)

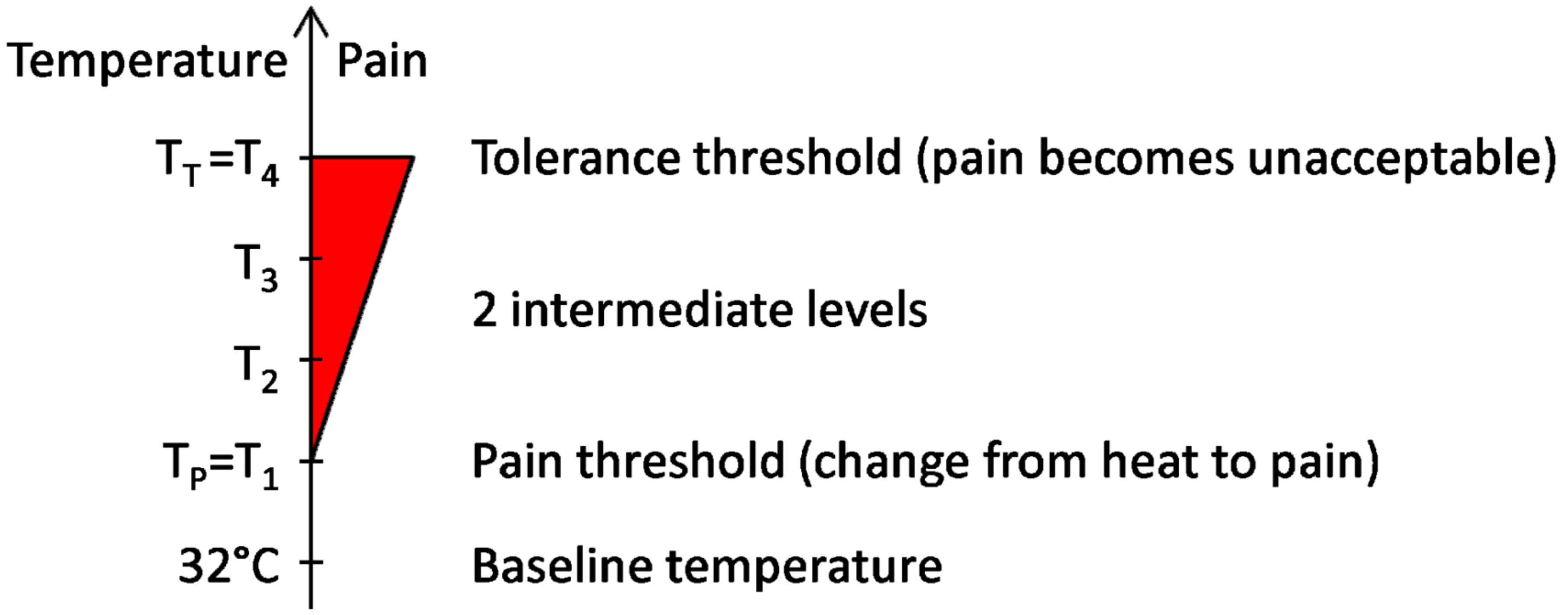
\+ video



Steffen Walter, Sascha Gruss, Hagen Ehleiter, Junwen Tan, Harald C Traue, Stephen Crawcour, Philipp Werner, Ayoub Al-Hamadi, and Adriano O Andrade. The biovid heat pain database data for the advancement and systematic validation of an automated pain recognition system. In 2013 IEEE International Conference on Cybernetics (CYBCO), pages 128–131. IEEE, 6 2013.

Personalized temperatures

- Temperature levels are ”personalized”, they are specific for each subject.
- All temperatures are <=50.5ºC.



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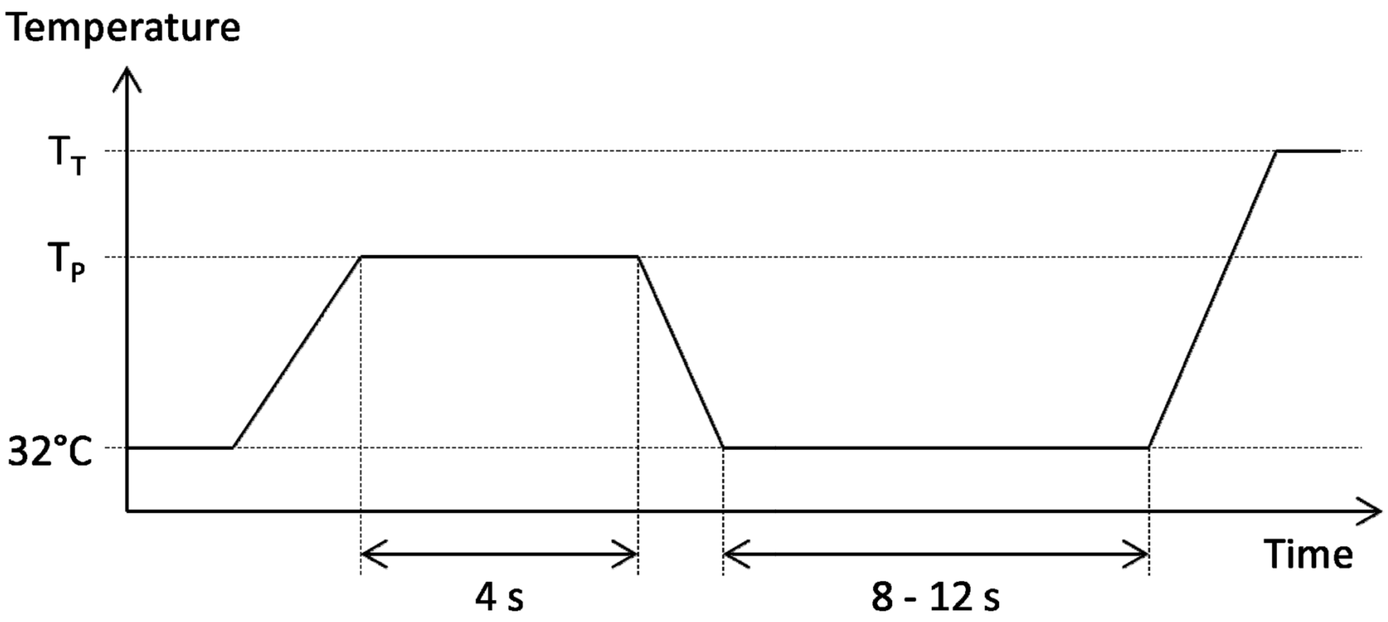
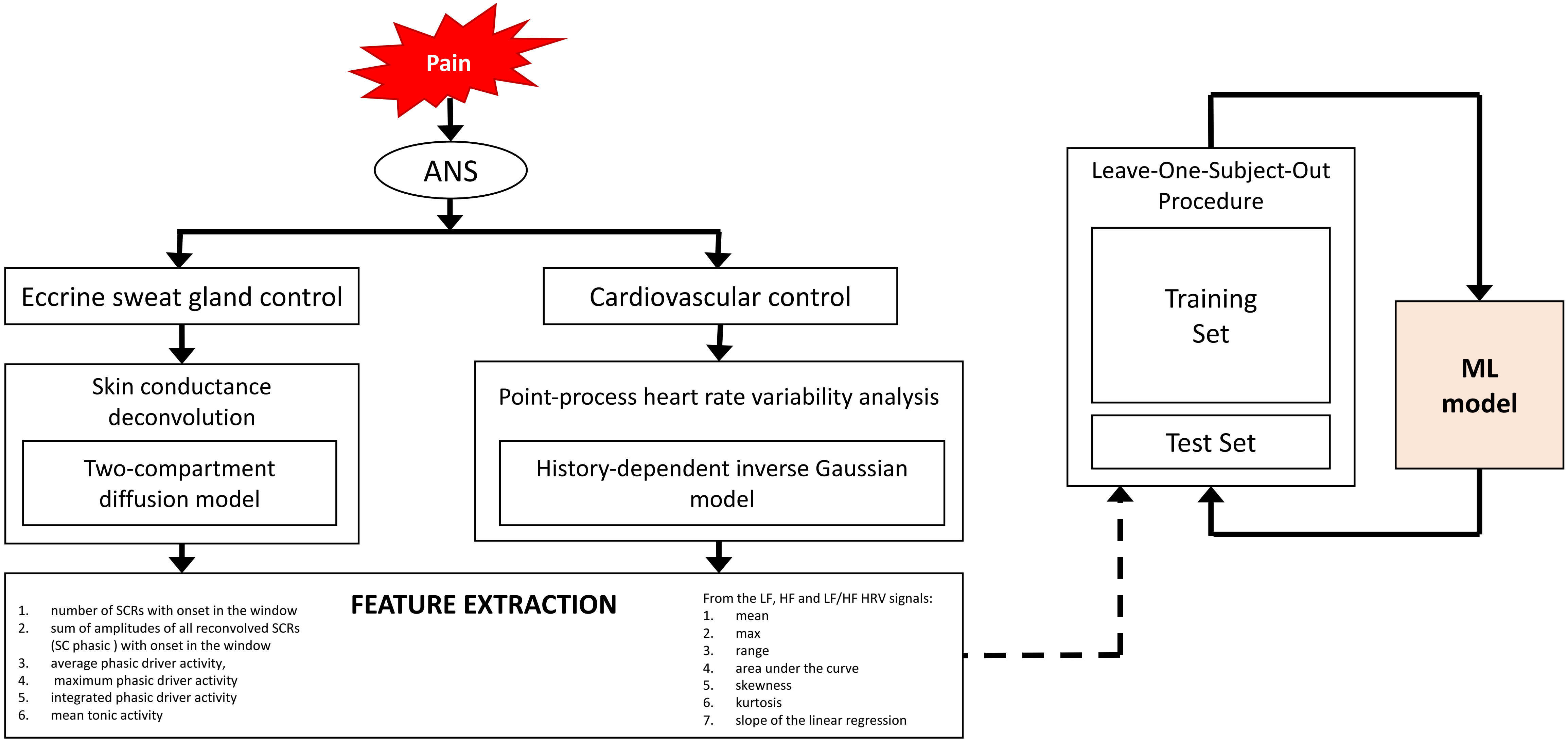
Pain stimulation



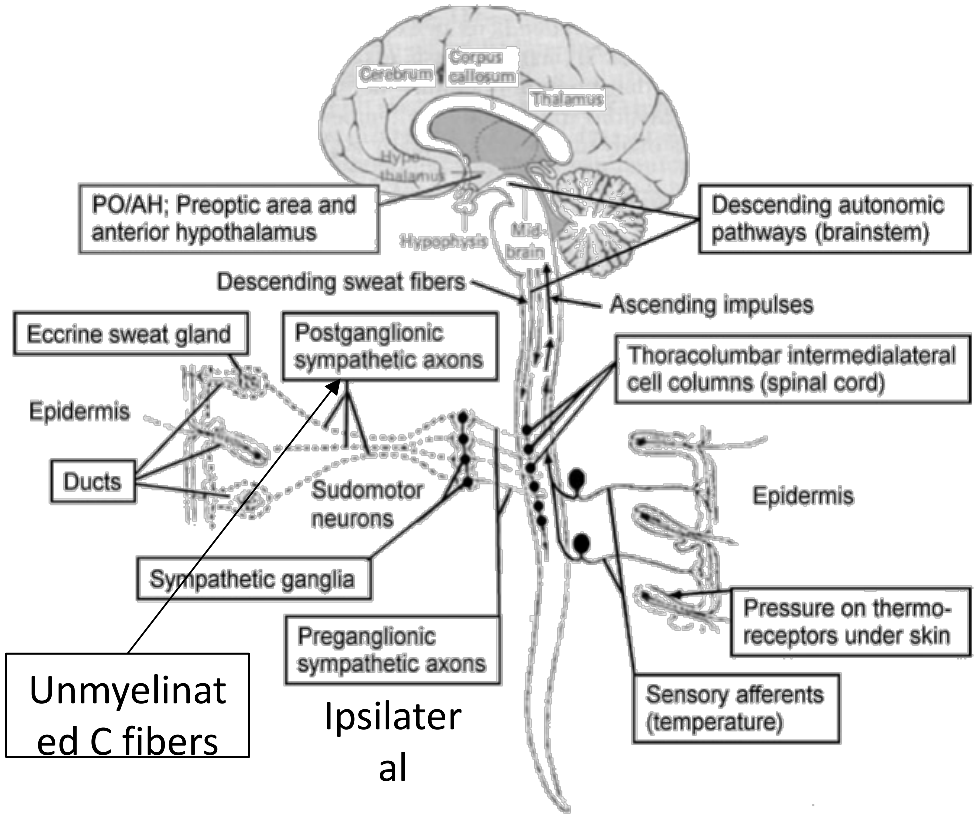
- Each sequence is 25 min approx.
- 80 stimulations, 20 for each temperature level.
- The maximum temperature of each pain level was hold for 4 s.
- The pauses between the stimuli were randomized between 8-12 s.

Steffen Walter, Sascha Gruss, Hagen Ehleiter, Junwen Tan, Harald C Traue, Stephen Crawcour, Philipp Werner, Ayoub Al-Hamadi, and Adriano O Andrade. The biovid heat pain database data for the advancement and systematic validation of an automated pain recognition system. In 2013 IEEE International Conference on Cybernetics (CYBCO), pages 128–131. IEEE, 6 2013.

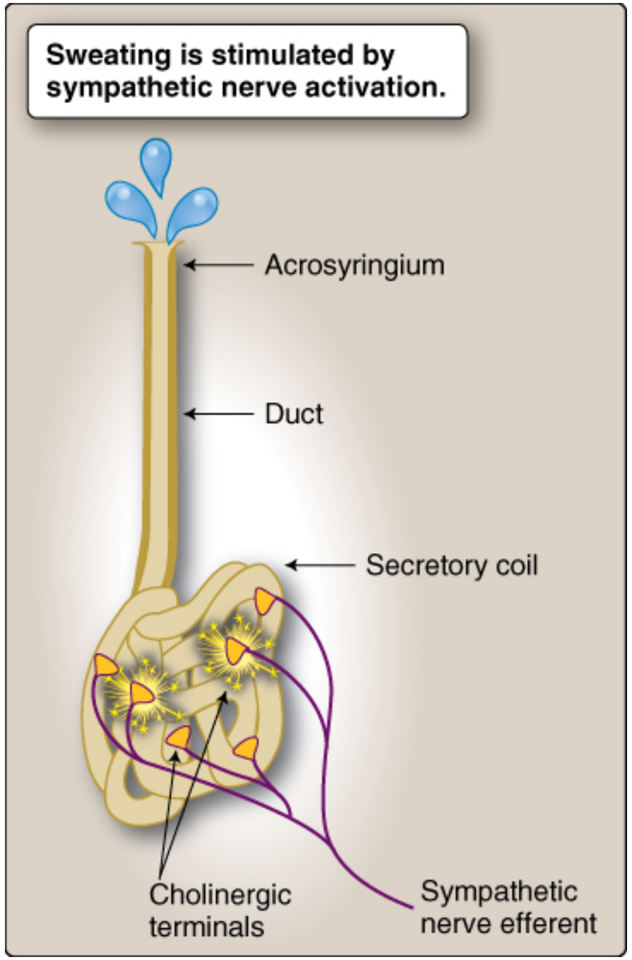
Pain intensity estimation model



Skin conductance responses (SCRs) represent sympathetic activity



Solely sympathetically regulated

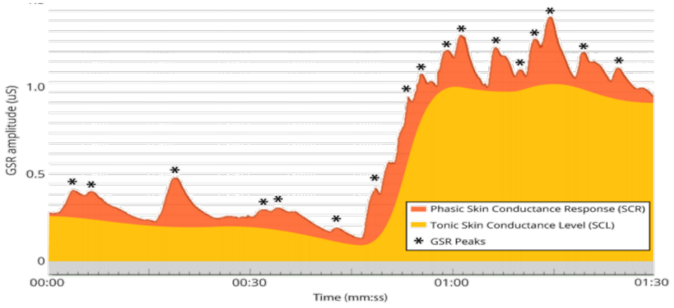


Innervation: sudomotor nerves (sympathetic nervous system)

Location: mainly foot, forehead, cheek, palm, and forearm.

Skin conductance responses: SCR amplitude is related to the number of recruited sweat glands.

- Each sudomotor unit innervates multiple sweat glands.
- Each sweat gland is innervated by many different fibers.

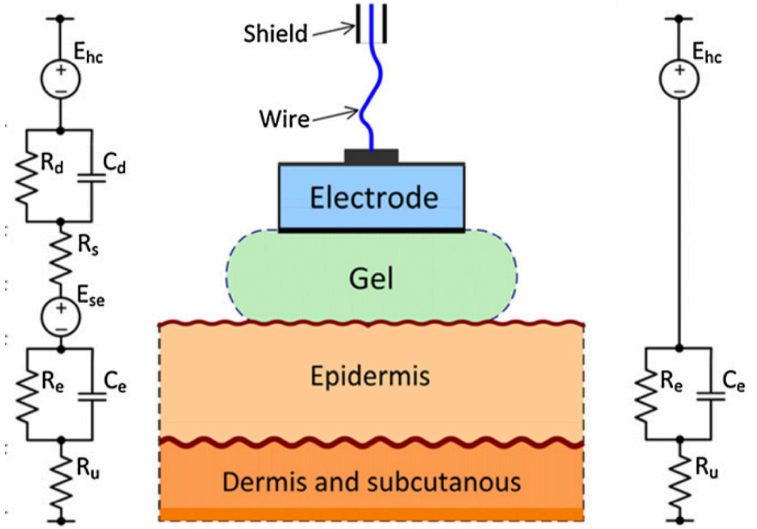


Tonic and phasic components

Measuring skin conductance

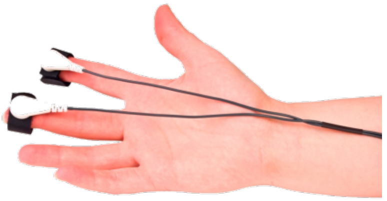
Non-wearable systems with gel electrodes

- Usually silver/silver chloride (Ag/AgCl).
- Use gel containing propylene glycol.
- Apply constant low voltage and measure current.



Wearable systems with dry electrodes

- Usually silver/silver chloride (Ag/AgCl).
- Can operate without gel. Depend on perspiration.
- Apply constant low voltage and measure current.

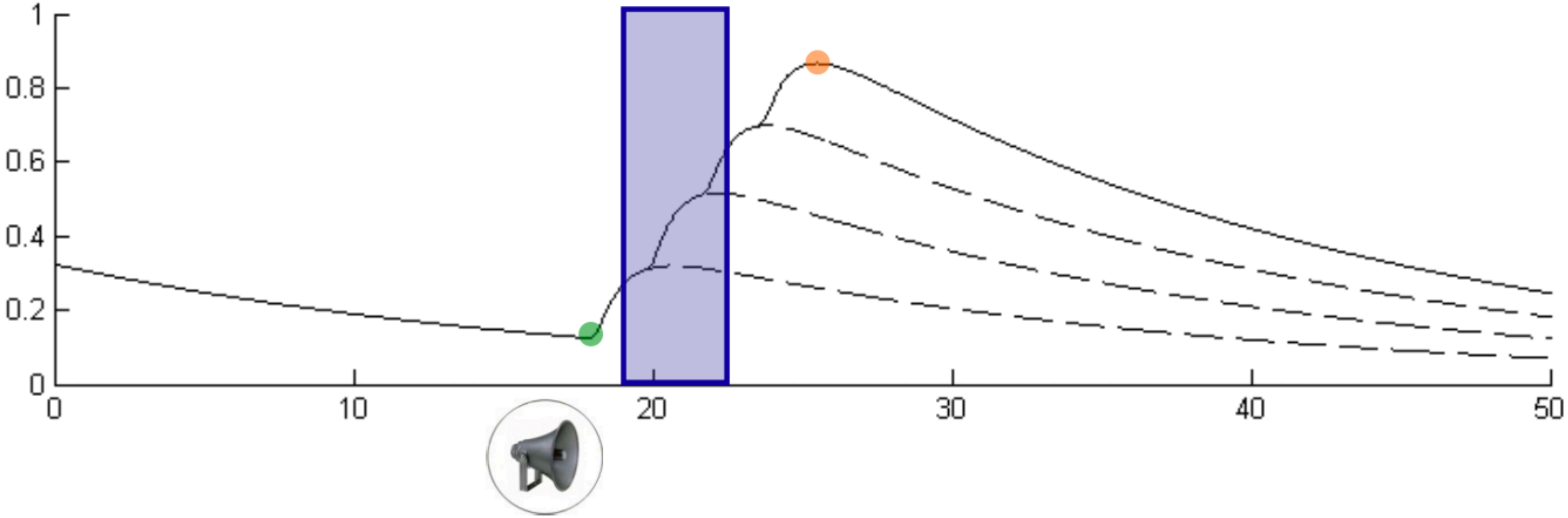


FlexComp Infiniti

Empatica E4

Empatica Embrace

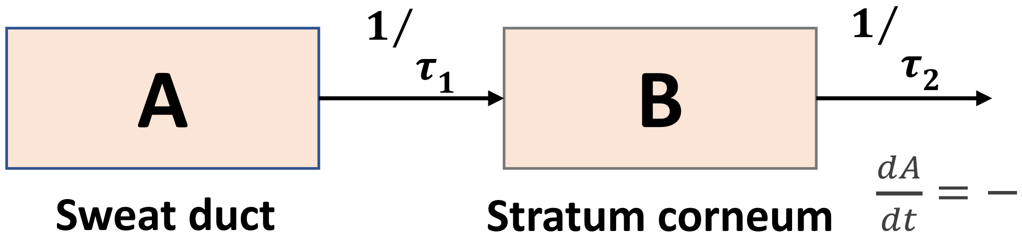
Closely spaced SCRs lead to signal superposition: skin conductance deconvolution is needed to differentiate responses



Standard methods result in underestimates of SCR amplitudes and rise times because they do not separate the different underlying SCRs, each driven by a sudomotor burst.

Skin conductance deconvolution: sweat diffusion model

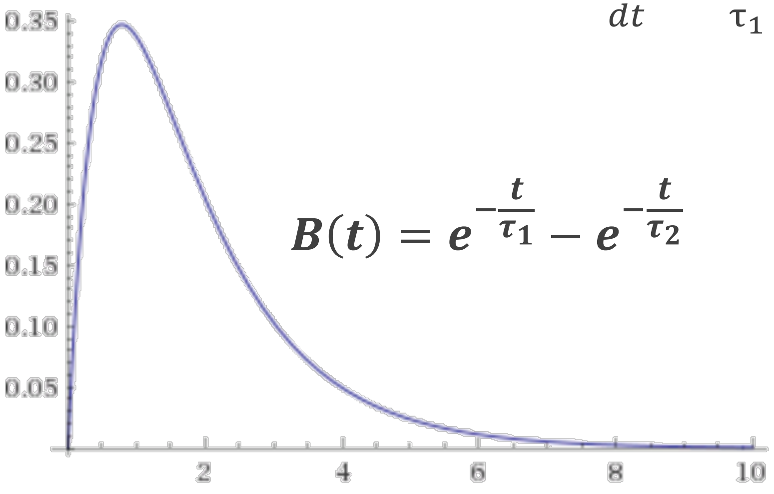
2 compartment model of sweat diffusion



$$\frac{dA}{dt} = -\frac{A(t)}{\tau_1}$$

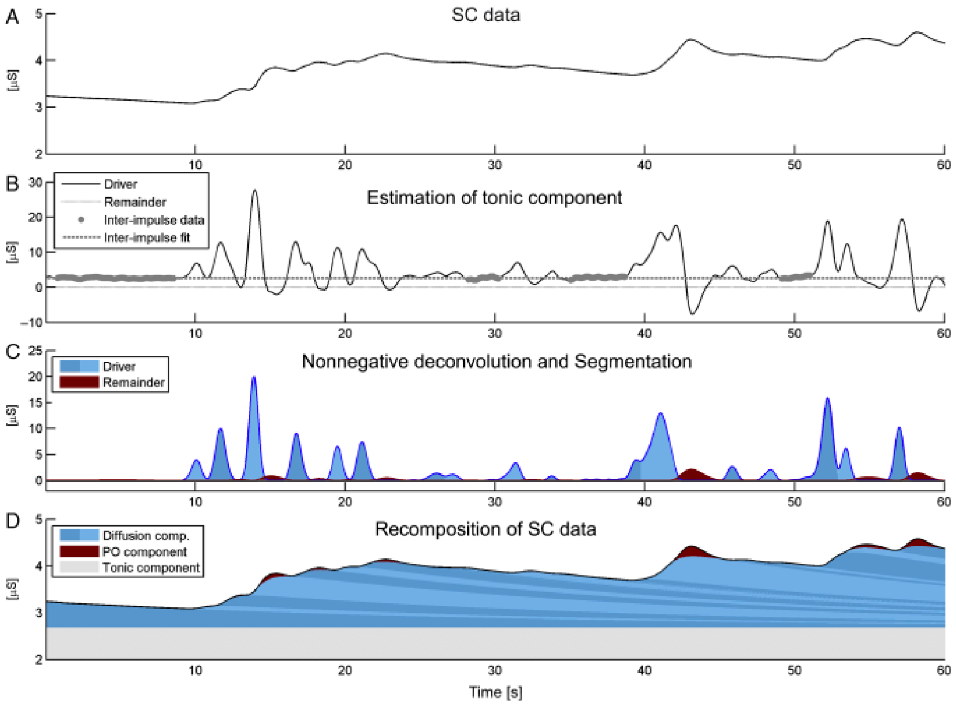
$$\frac{dB}{dt} = \frac{A(t)}{\tau_1} - \frac{B(t)}{\tau_2}$$

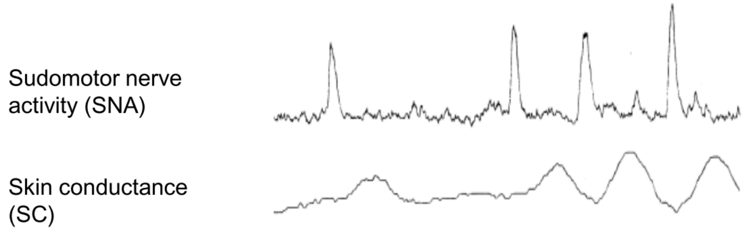
Impulse Response Function (IRF)



$$B(t) = e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}}$$

$$\boxed{\mathrm{SC} = \mathrm{SC}_{\mathrm{tonic}} + \mathrm{SC}_{\mathrm{phasic}} = \mathrm{SC}_{\mathrm{tonic}} + \mathrm{Driver}_{\mathrm{phasic}} * \mathrm{IRF}}$$

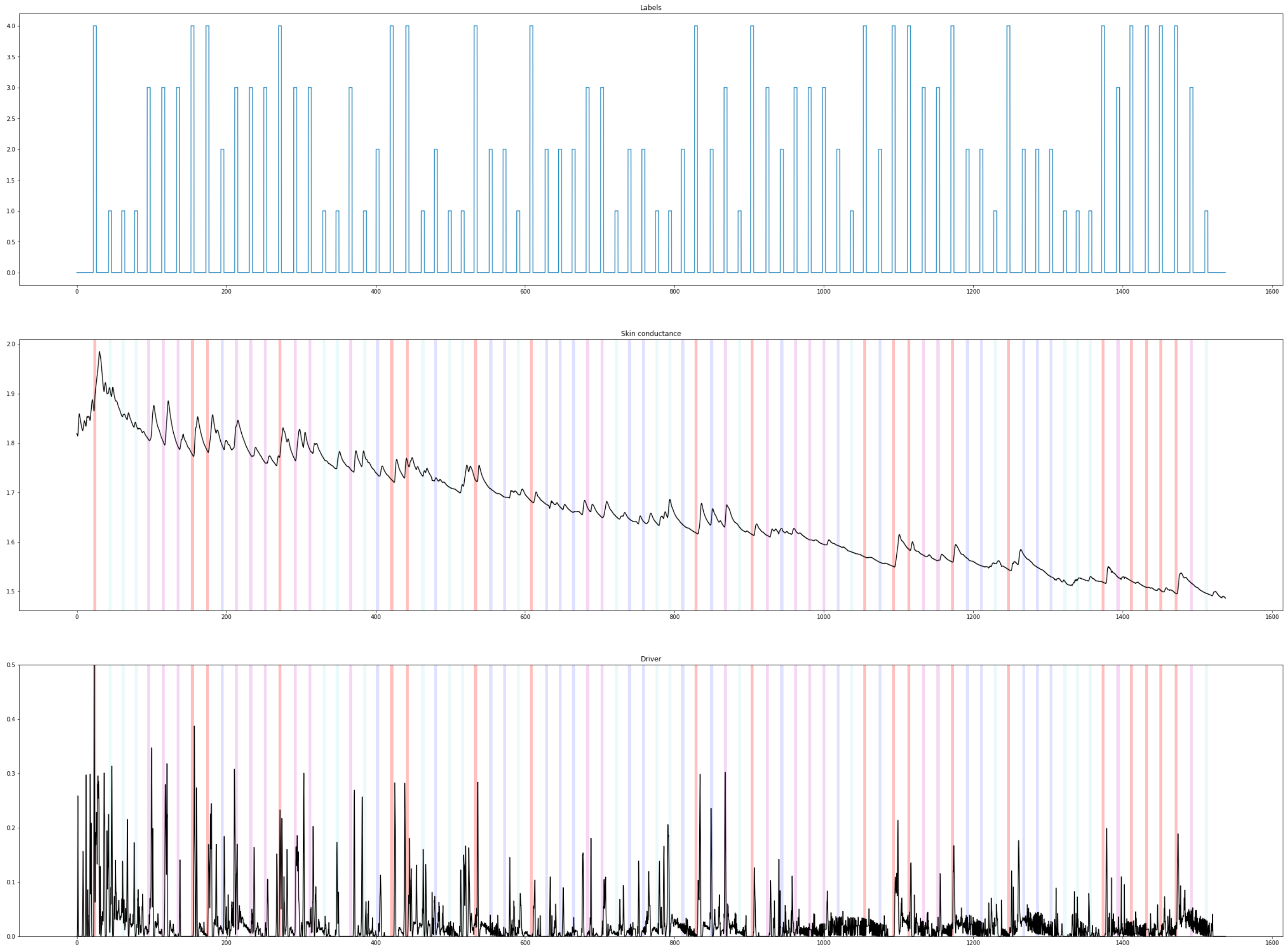




(Macefield & Wallin, 1996)

M. Benedek and C. Kaernbach, “Decomposition of skin conductance data by means of nonnegative deconvolution,” Psychophysiology, vol. 47, pp. 647–658, 2010.

Skin conductance deconvolution can extract the phasic driver, a correlate for sudomotor neuron activity



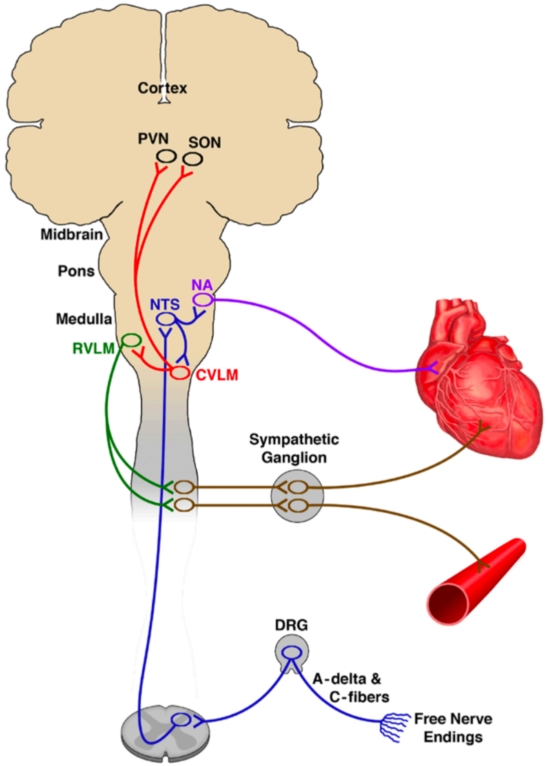
← Pain labels
(0 = no pain, 4 = max pain)

← Skin conductance

$$\boxed{SC = SC_{\text{tonic}} + SC_{\text{phasic}} = SC_{\text{tonic}} + \text{Driver}_{\text{phasic}} * \text{IRF}}$$

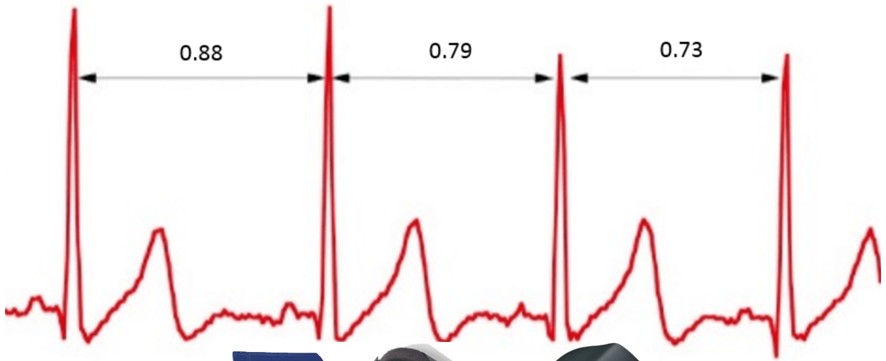
← Phasic driver

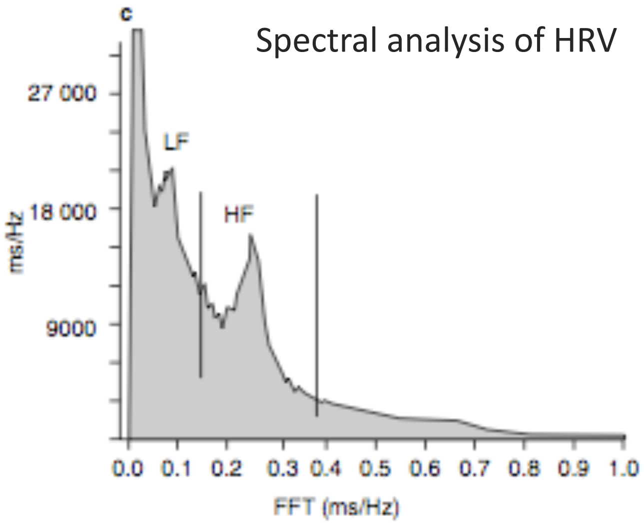
Heart rate variability (HRV) can be used to infer sympathetic/parasympathetic activity



Nociceptive Medullary Autonomic Circuit

General Anesthesia, Sleep, and Coma (NEJM '10)





HF (0.15-0.4 Hz)	LF (0.04-0.15 Hz)	VLF (0.004-0.04 Hz)
Parasympathetic only	Sympathetic and parasympathetic	Thermoregulation and baroreflex

Pain can be measured by HRV analysis as **increase in LF spectral content** (+sympathetic) and **decrease in HF spectral content** (- parasympathetic)

Point-Process HRV
Interbeat Interval Probability Model

Probability of observing the next beat ($t > t_n^R$) follows an Inverse Gaussian distribution of mean $\mu_{RR}(t)$ and shape parameter $\lambda_{RR}(t)$:

$$f_{\mathrm{RR}}(t) = \sqrt{\frac{\lambda_{\mathrm{RR}}(t)}{2\pi[t - t_{\mathrm{n}}^{\mathrm{R}}]^3}} \exp\left(-\frac{\lambda_{\mathrm{RR}}(t)[t - t_{\mathrm{n}}^{\mathrm{R}} - \mu_{\mathrm{RR}}(t)]^2}{2\mu_{\mathrm{RR}}^2(t)[t - t_{\mathrm{n}}^{\mathrm{R}}]}\right)$$

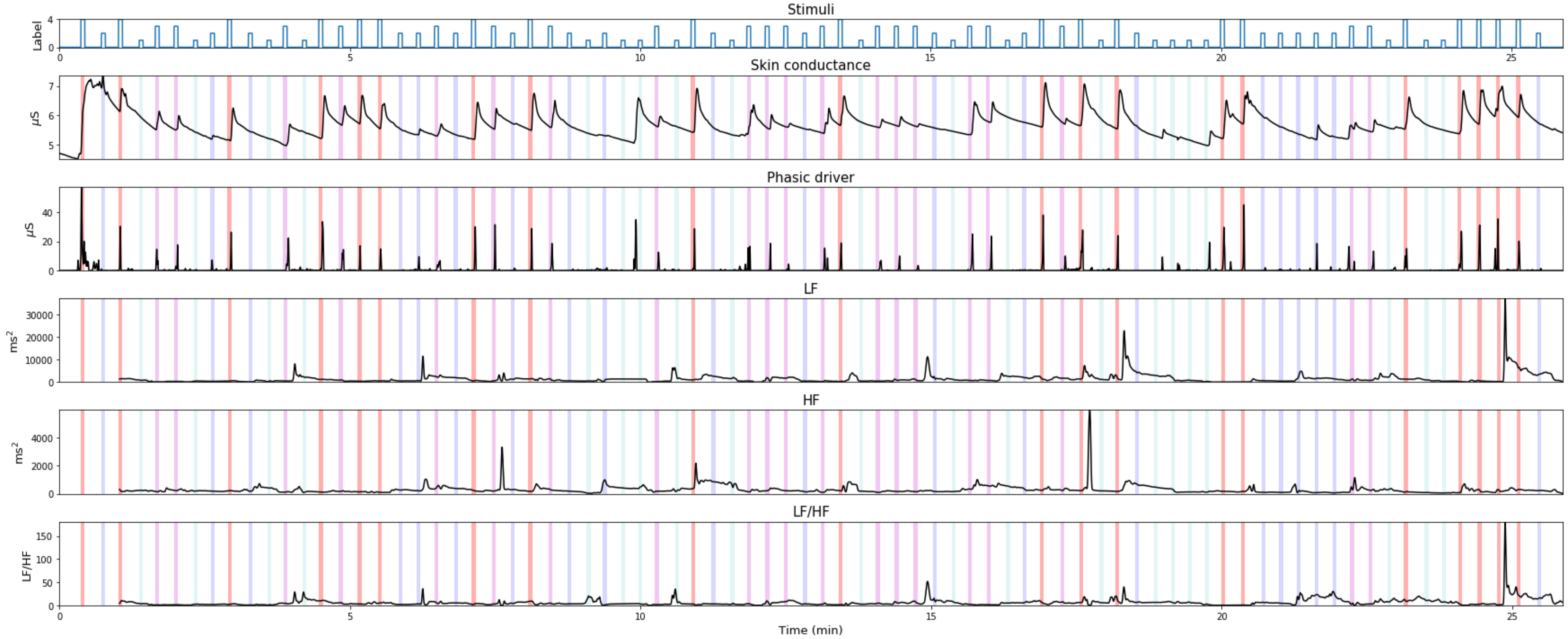
$\boldsymbol{\mu_{RR}(t)}$ is a linear function of P past heart period $w_n^R = t_{n+1}^R - t_n^R$
→ History dependent Inverse Gaussian

$$\mu_{\mathrm{RRI}}(t) = a_0^{(1)}(t) + \sum_{\mathrm{k}=1}^{\mathrm{P}} a_{\mathrm{k}}^{(11)}(t) w_{\mathrm{n-k}}^{\mathrm{RRI}}$$

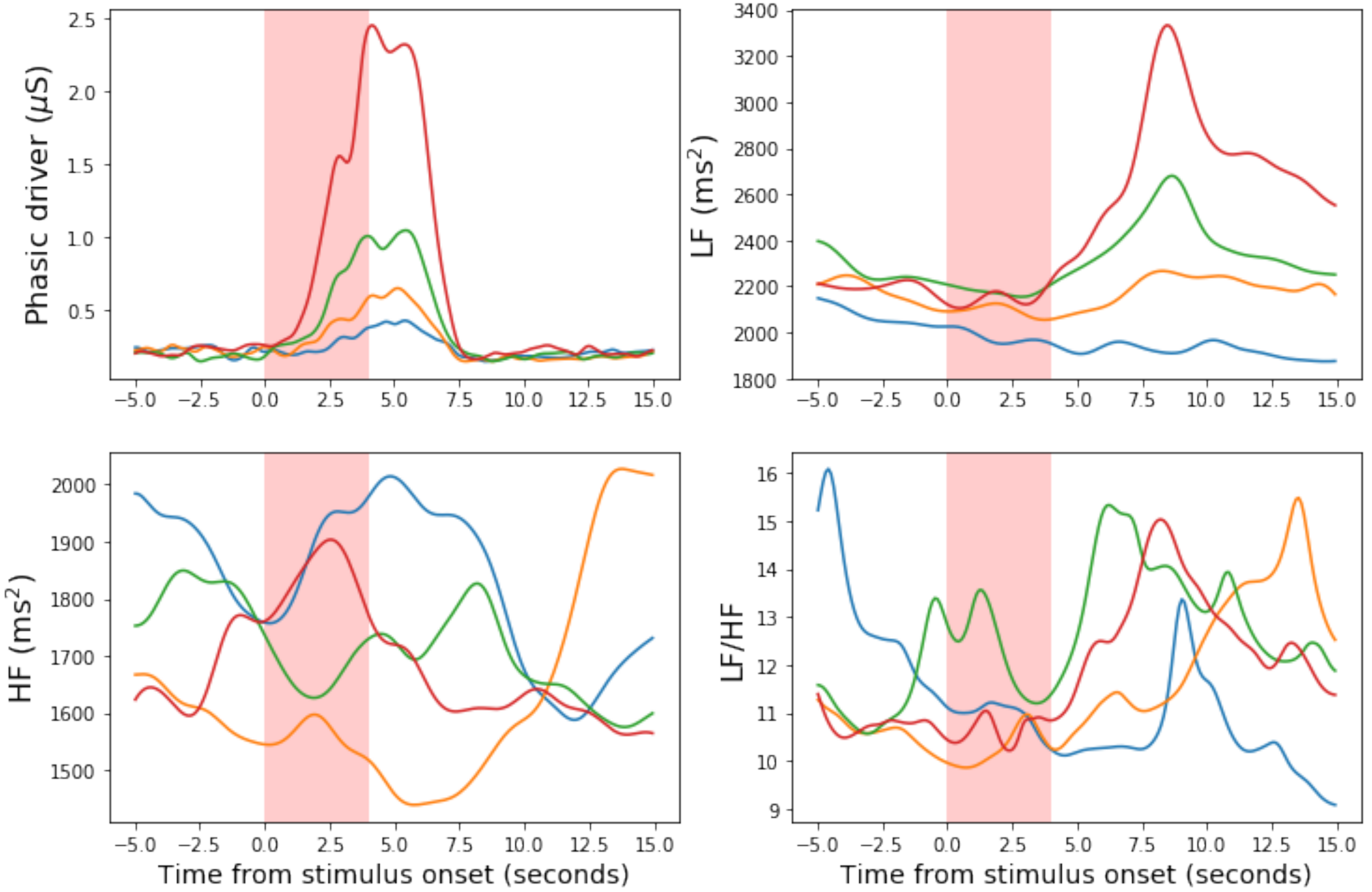
$\{\mu_{RR}(t), \lambda_{RR}(t)\}$ → Maximization of **local likelihood**

R. Barbieri and E. Brown, "Analysis of Heartbeat Dynamics by Point Process Adaptive Filtering," IEEE Transactions on Biomedical Engineering, vol. 53, no. 1, pp. 4–12, 1 2006.
Code available here: users.neurostat.mit.edu/barbieri

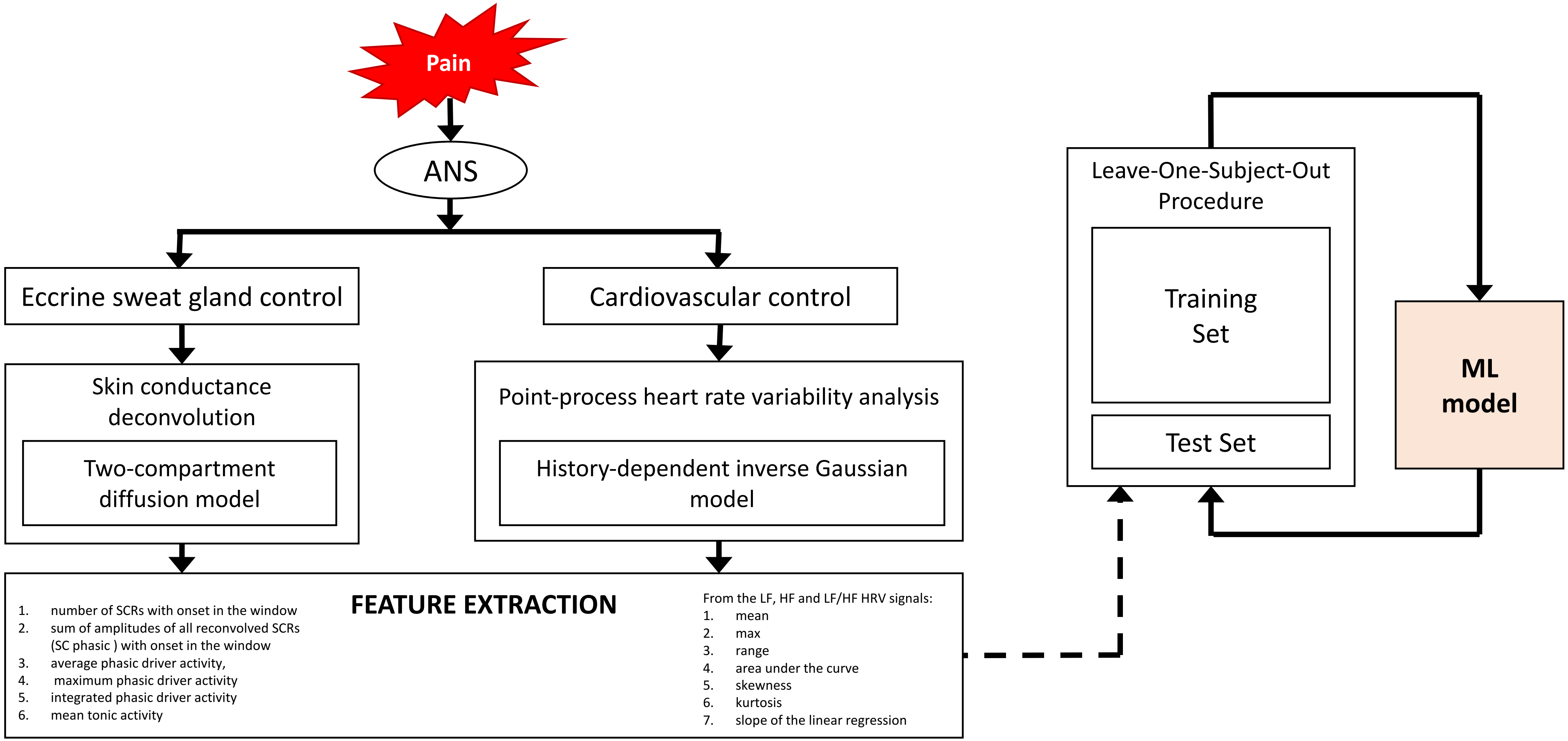
BioVid Heat Pain Dataset – example of recording



Average SC and HRV changes with pain over the entire population



Pain intensity estimation model



Results on the BioVid Heat Pain Database

Binary classification

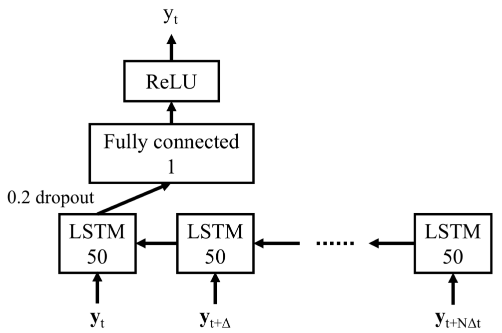
- No pain (BLN) vs P4, win_{SC}=6sec and win_{HRV}=8sec

Feature set	Accuracy		
	Logistic regression	SVM linear	SVM RBF
SC	**74.21(17.54)**	**72.88(17.23)**	**67.57(12.91)**
HRV LF	57.69(09.34)	55.92(09.57)	51.54(08.19)
HRV HF	50.10(08.03)	50.24(08.63)	49.81(05.04)
HRV LF/HF	53.15(09.56)	50.82(05.45)	47.18(03.67)
SC+HRV	71.89(18.90)	72.20(16.10)	62.07(19.72)

- No pain (BLN) vs P1/P2/P3/P4 with SC features only.

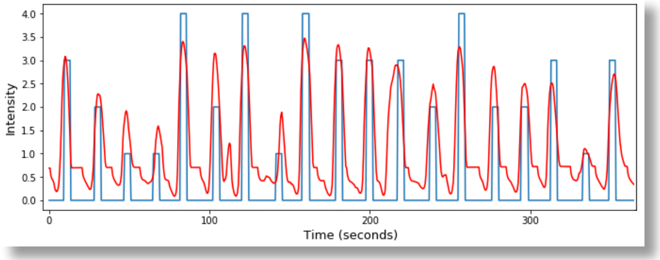
Binary classification task	Accuracy		
	Logistic regression	SVM linear	SVM RBF
BLN vs P4	**74.21(17.54)**	72.88(17.23)	67.57(12.91)
BLN vs P3	**66.00(14.83)**	64.14(14.51)	63.60(11.88)
BLN vs P2	**59.40(12.61)**	58.20(13.99)	58.46(10.04)
BLN vs P1	54.57(10.90)	55.30(10.46)	**56.44(09.35)**

Regression (SC)



LSTM neural network

10 win of duration 5 sec with Δt=0.5



Regression of stimuli

Algorithm	MAE	RMSE	R^2
Linear Regression	1.16(0.07)	1.36(0.09)	0.06(0.14)
SVR linear	1.15(0.08)	1.37(0.12)	0.05(0.21)
SVR RBF	1.11(0.14)	1.33(0.14)	0.11(0.19)
NR-NN	1.12(0.10)	1.32(0.10)	0.12(0.12)
R-NN	1.07(0.15)	**1.29(0.17)**	0.22(0.20)
LSTM-NN	**1.05(0.15)**	**1.29(0.16)**	**0.24(0.19)**

Thanks!

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