28th Annual Gabor Racz Advanced Interventional Pain Conference and Workshop
Budapest, Hungary August 25-27, 2025

Arms Race in Closed Loop SCS

Dr Simon Thomson MBBS FIPP FFPMRCA

Consultant in pain medicine and neuromodulation

Mid & South Essex University Hospitals NHS

Potential Conflicts of Interest

- Scientific Advisory Board: Boston Scientific, Galvani Bioelectronics, Mainstay Medical, Saluda Medical
- Scientific Research: MSE/BTUH R&D – NIHR, Boston Scientific, Mainstay Medical, Saluda Medical
- Speaker's Bureau: Boston Scientific, Mainstay Medical, Saluda Medical
- Stock Holder: None
- Stock Options: None
- Product Royalties: None
- Employed by
  - National Health Service, UK.

Commercially available Closed Loop SCS

- Saluda Medical Evoke
- Medtronic Inceptiv
- Other manufacturers are looking at their ideas around Sensing and Closed loop
- Investment decisions based upon
  - Added value
  - Competition

Agenda

- Mechanisms of Action of SCS
- The Evoked Compound Action Potential – ECAP
- How ECAPS can optimize therapy

Pillars for successful SCS outcomes

Patient selection Multi-professional team E-Tool	High quality implant techniques	Good follow-up access, Care pathway implementation and programming	Advanced SCS/NM Technology

https://scstool.org

www.scstool.org

Gate Control Theory

19 November 1965, Volume 150, Number 3699

SCIENCE

Pain Mechanisms: A New Theory

A gate control system modulates sensory input from the skin before it evokes pain perception and response.

Ronald Melzack and Patrick D. Wall

Gate Control Theory of Pain

Stimulation of the skin evokes nerve impulses that are transmitted to three spinal cord systems (Fig. 3): the cells of the substantia gelatinosa in the dorsal horn, the dorsal-column fibers that project toward the brain, and the first central transmission (T) cells in the dorsal horn. We propose that (i) the substantia gelatinosa functions as a gate control system that modulates the afferent patterns before they influence the T cells; (ii) the afferent patterns in the dorsal column system act, in part at least, as a central control trigger which activates selective brain processes that influence the modulating properties of the gate control system; and (iii) the T cells activate neural mechanisms which comprise the action system responsible for response and perception. Our theory proposes that pain phenomena are determined by interactions among these three systems.

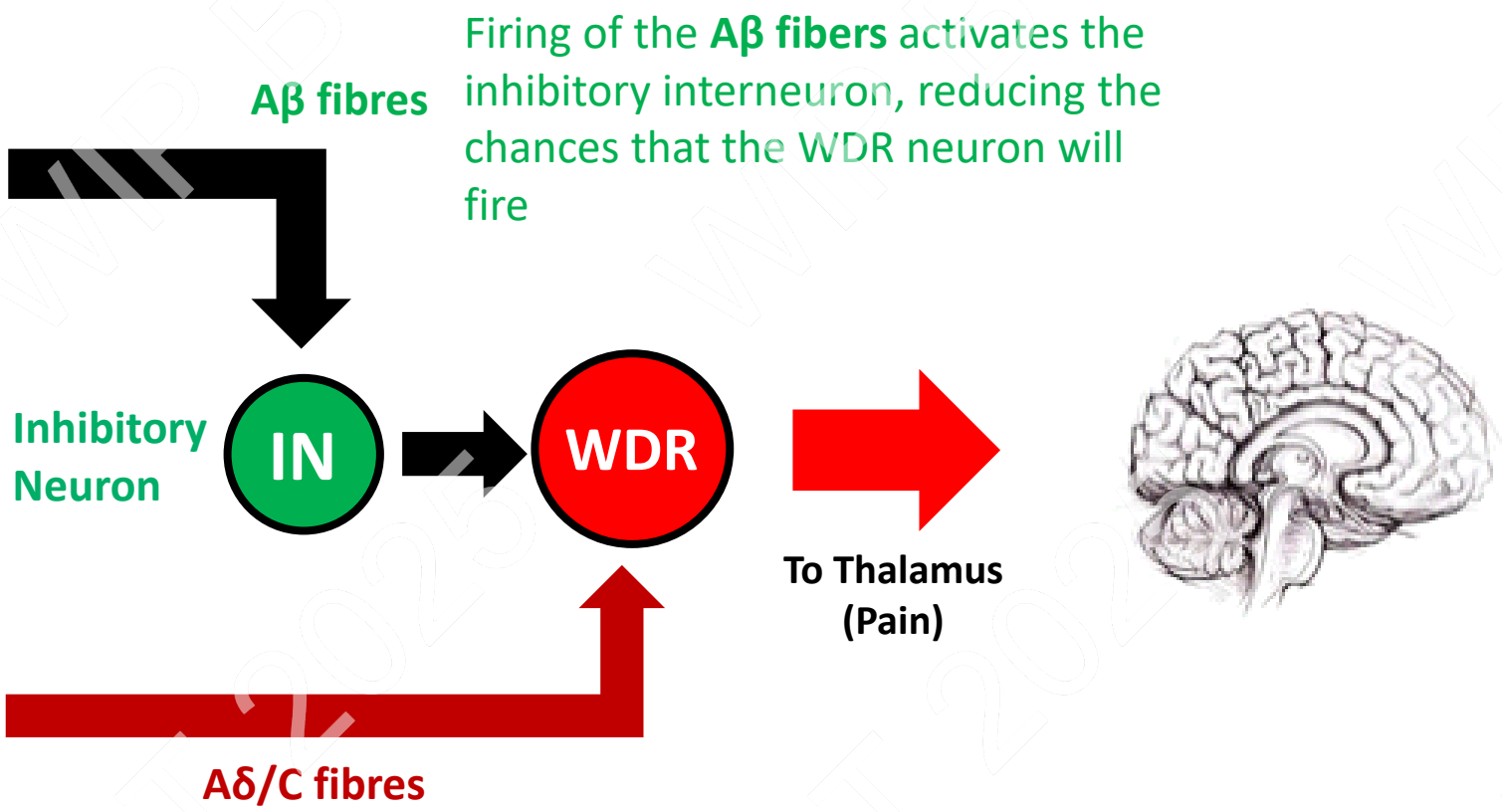
What do you do?

- You stub your toe on a piece of furniture…
- You accidentally bang your head…
- Your child bruises their elbow after taking a tumble…

"Gate control is why rubbing an injury works"
"It accounts for the lack of proportionality of pain experience and observed pathology"

Pain Relief with SCS starts with neural activation

Gate Control Theory – in the spinal cord



- Aδ fibers carry fast/discriminatory pain
- C fibers carry slow pain

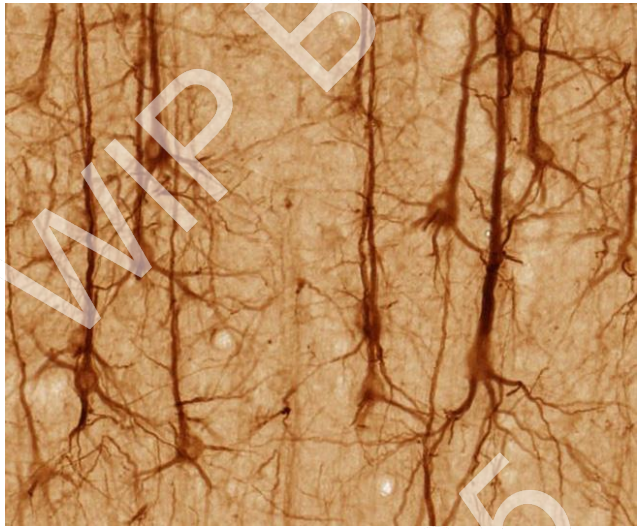
Melzack & Wall[1]

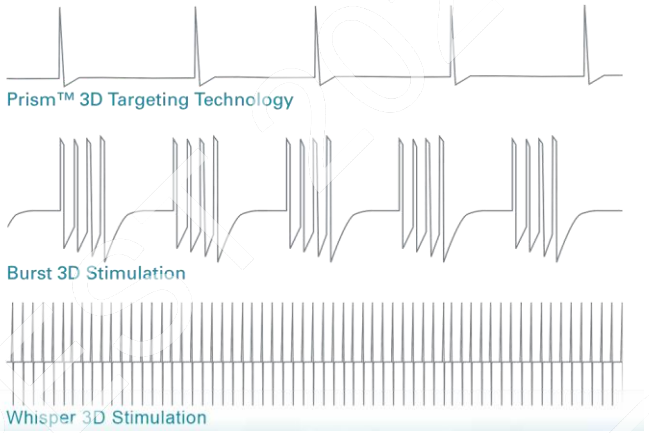
WDR = Wide Dynamic Range neuron

What is Neuromodulation?

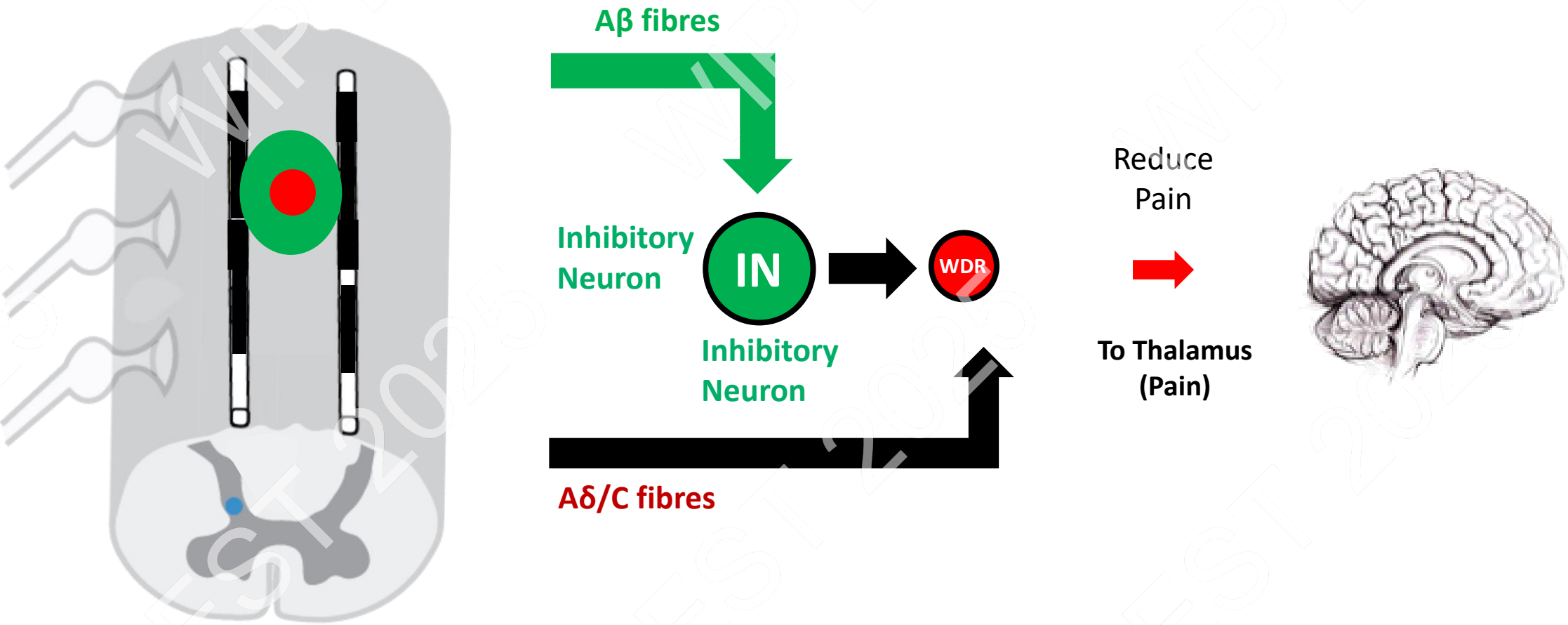
Neuromodulation can be defined as the modification (modulation) of nerve (neuro) activity through targeted delivery of a stimulus.

The stimulus is usually electrical but can be targeted pharmacology (intrathecal drug delivery), light (optogenetics)



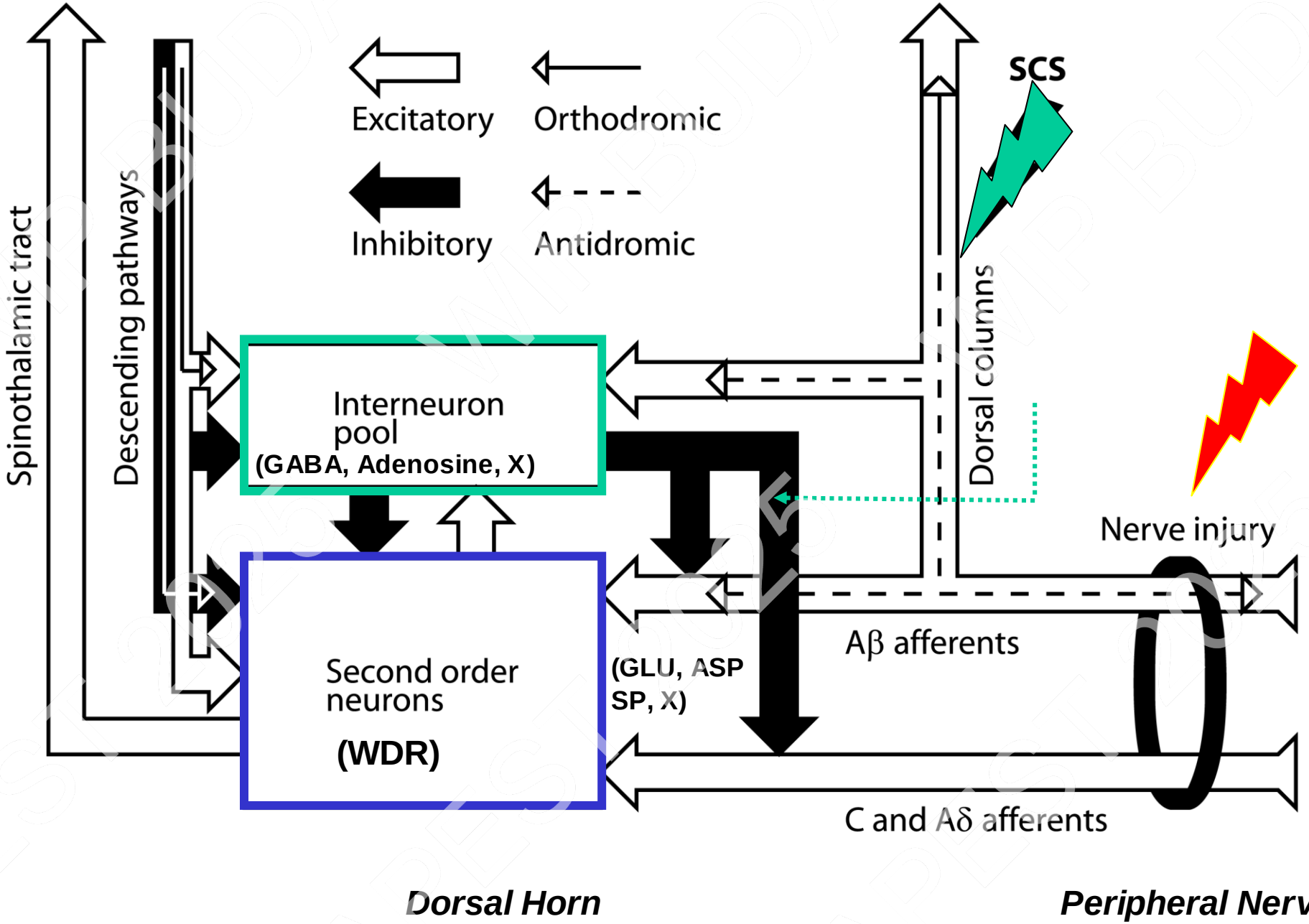


Spinal cord stimulation (SCS)



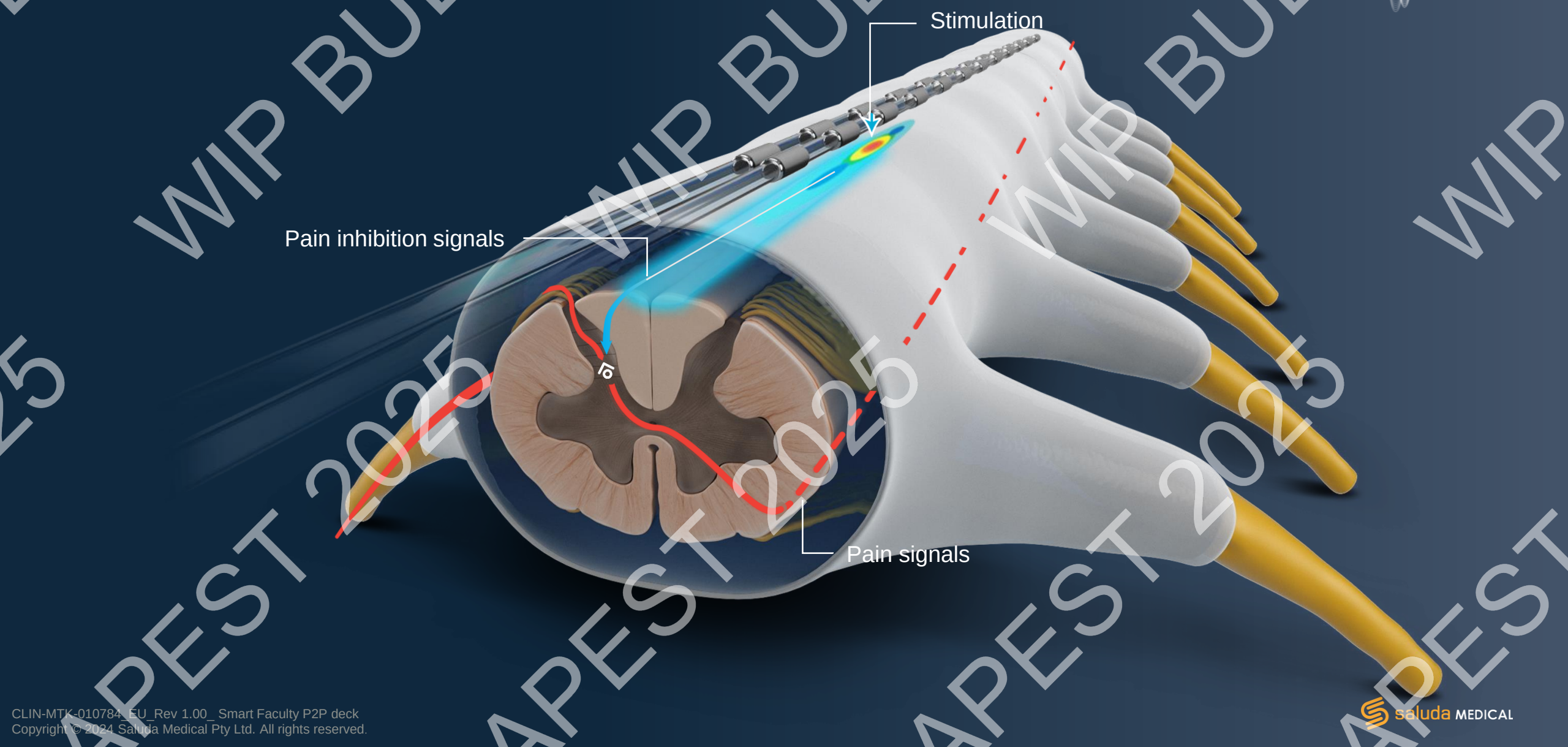
FAST™ MOA based on computational modeling from Dr. Warren Grill's lab at Duke University. Gilbert et al., Computational modeling predicts dorsal columns are involved in fast-acting sub-perception spinal cord stimulation (SCS). SFN 2021

Melzack & Wall[1] Hillman & Wall


Excitatory
Orthodromic
Inhibitory
Antidromic
Spinothalamic tract
Descending pathways
Interneuron pool
(GABA, Adenosine, X)
Second order neurons
(WDR)
(GLU, ASP SP, X)
SCS
Dorsal columns
Nerve injury
Aβ afferents
C and Aδ afferents
Dorsal Horn
Peripheral Nerve

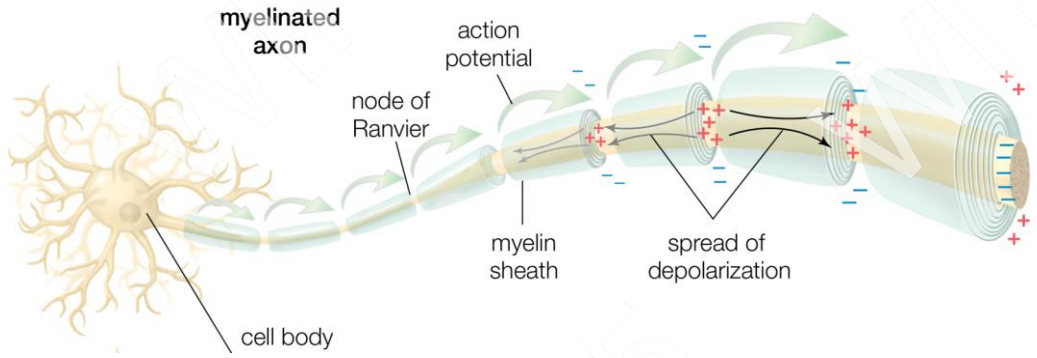
Saluda Medical Evoke

Pain relief in SCS is driven by dosing of the spinal cord

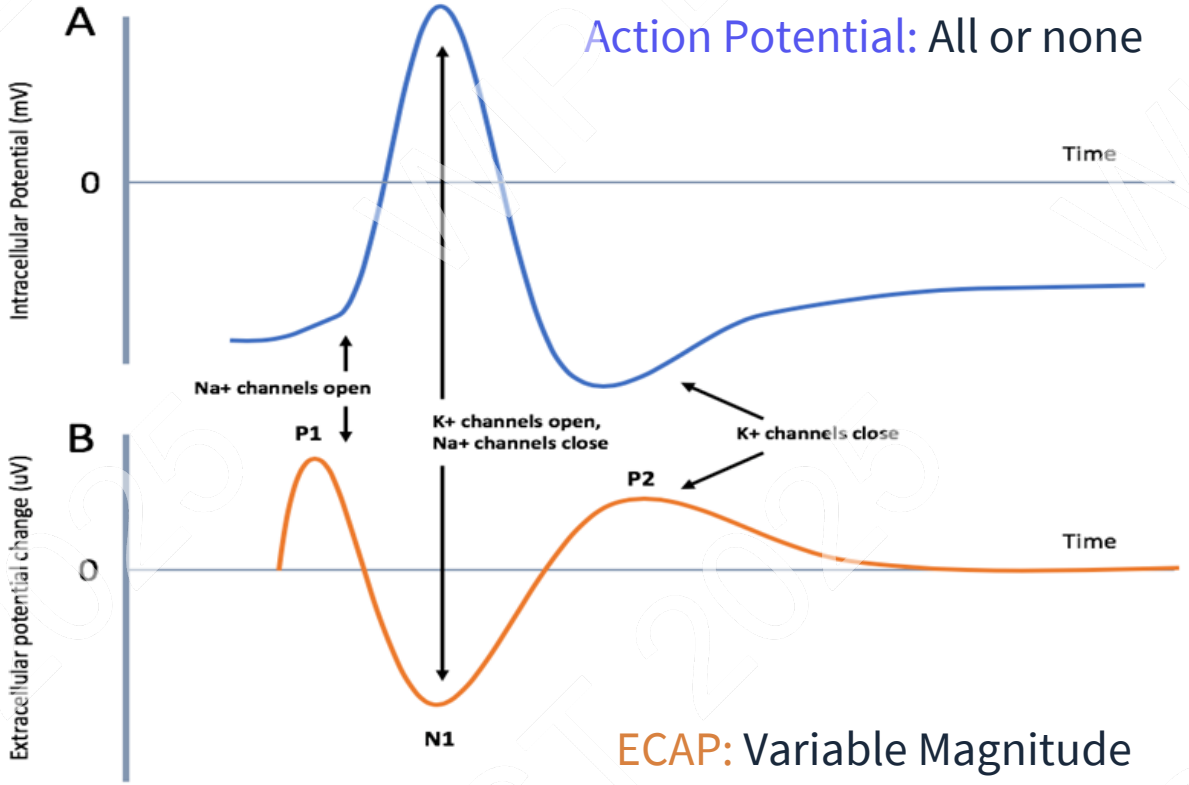


saluda MEDICAL

Evoked Compound Action Potentials (ECAPs):
A Window into Spinal Cord Activation



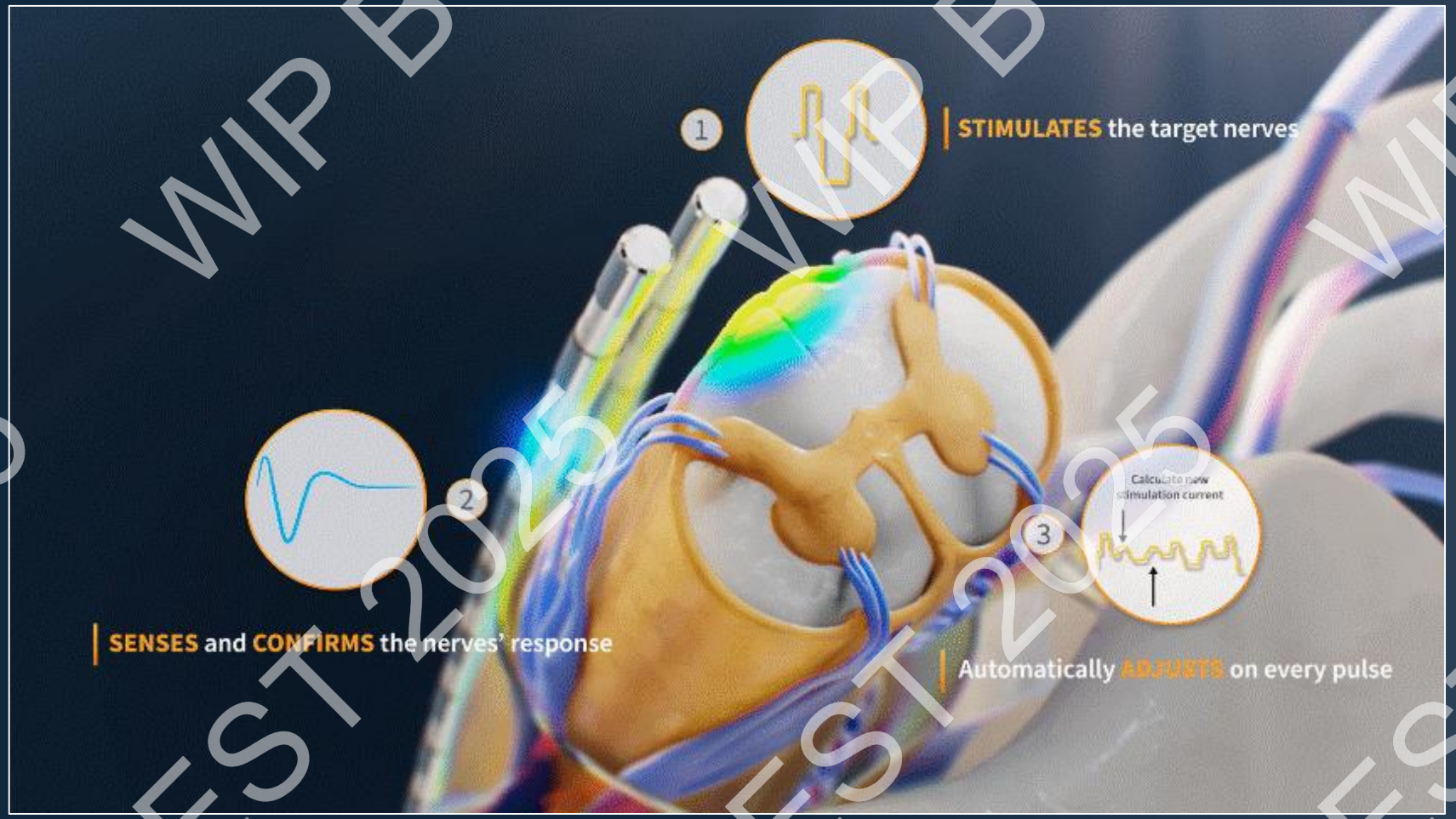
An ECAP is the extracellular measurement of the sum of the action potentials of the fibers being recruited ***with stimulation***



Action Potential: All or none

ECAP: Variable Magnitude

SmartLoop® Dose-Control Technology senses and confirms the nerves' response AND automatically adjusts on every pulse

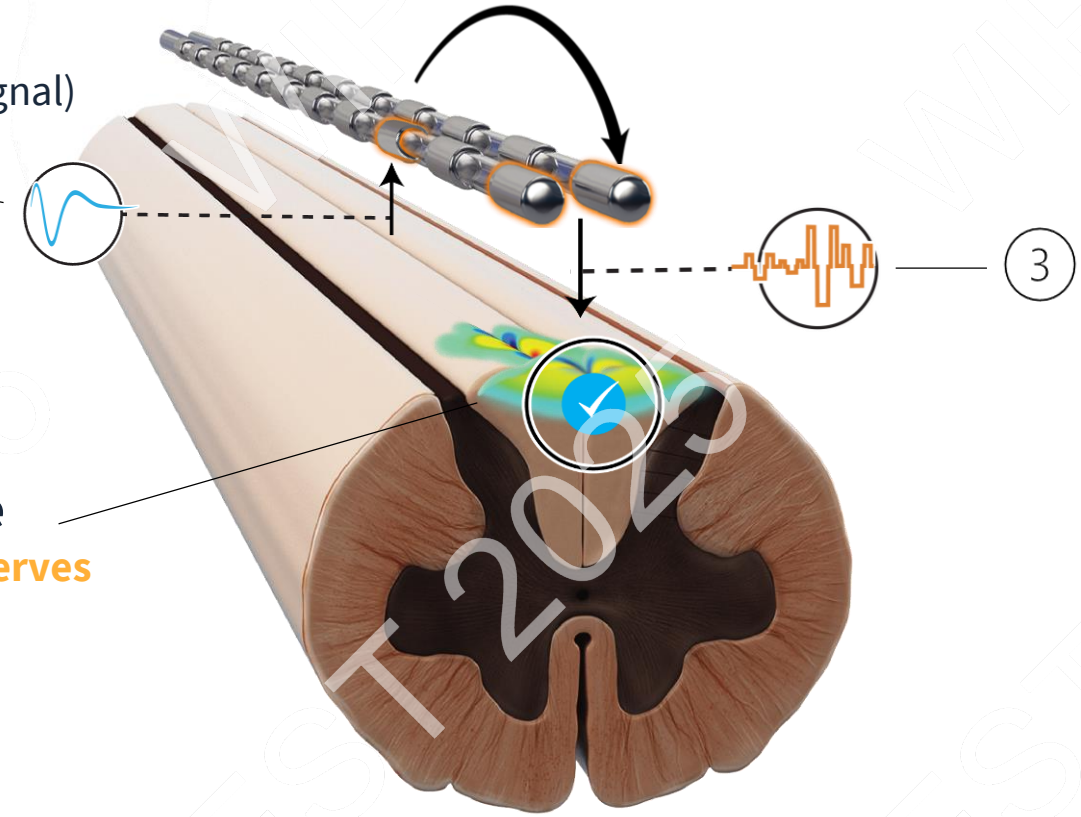


1. Stimulate the target nerves
2. Sense and Confirm the nerves' response
3. Automatically adjust on every pulse

saluda MEDICAL

…By Closing the Loop

2 **Sense**
the nerves' response (ECAP signal) in real time to **measure** and **confirm activation**



3 **Auto-adjust**
stimulation on **every pulse** (4+ million times per day[1]) to maintain activation

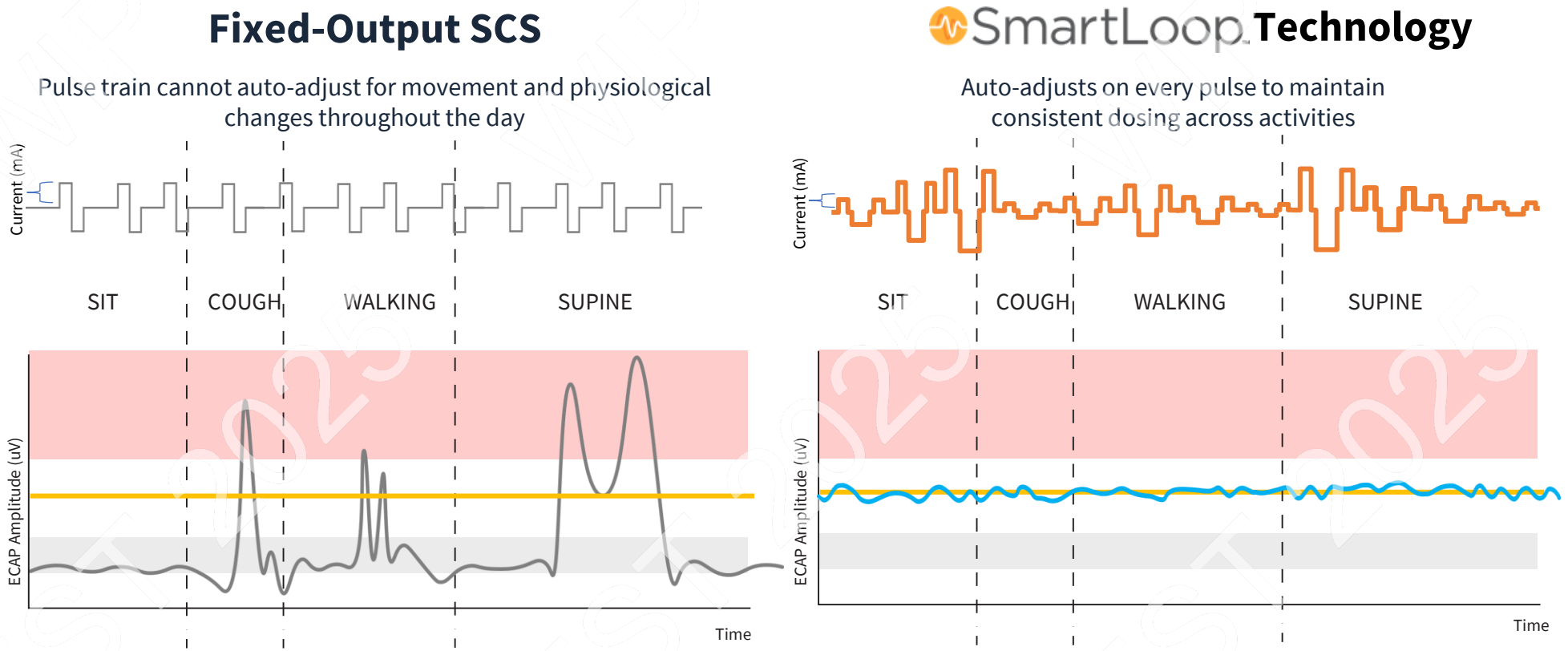
1 **Stimulate**
the **target nerves**

1. Stimulation adjustments are made at the same rate as frequency. 4+ million adjustments per day is based on 50Hz.

The SCS dose delivered varies with position, breathing, coughing

- Dorsal columns
- The volume of tissue activated
  - Varies with electrode cord electrical field and proximity
- This occurs with all Fixed Output SCS
- Changes in Volume of Tissue Activated may result in
- Over and Under Stimulation
  - Inconsistent Outcomes
  - Poor patient satisfaction
  - Therapy habituation

SmartLoop® Technology sets an ECAP target dose and auto-adjusts on every pulse to maintain consistent pain relief



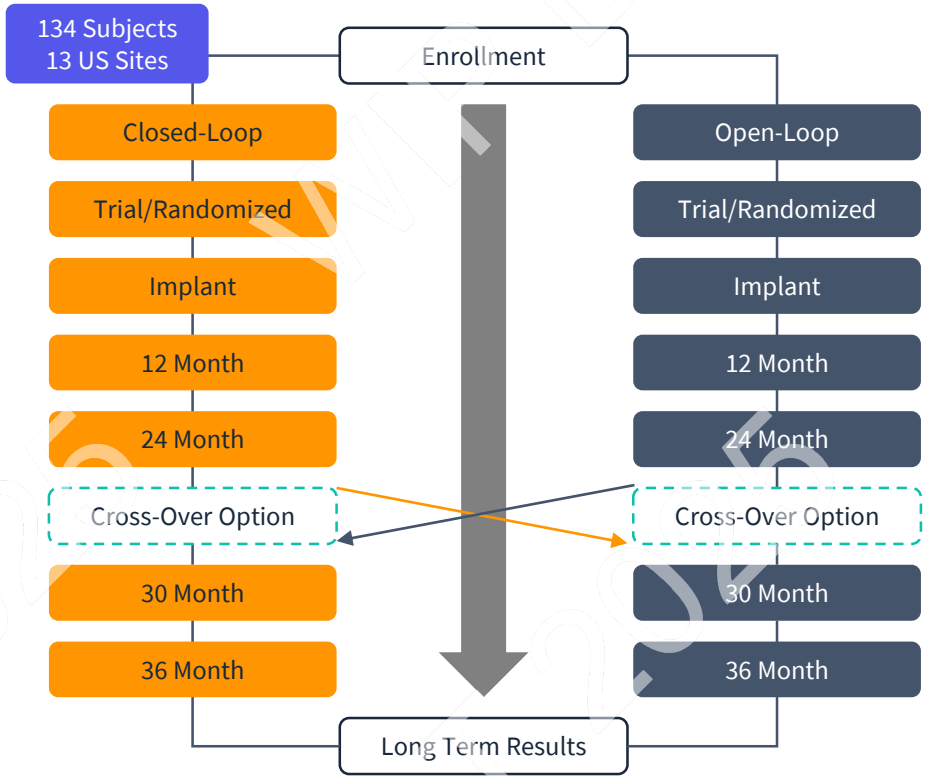
Landmark EVOKE IDE Study

- Landmark **Double-Blinded RCT**
- Self-selected **Crossover**
- Longest-term RCT data in SCS with published **36-month** outcomes

>80MM
Baseline VAS (average)

>11Y
years of pain

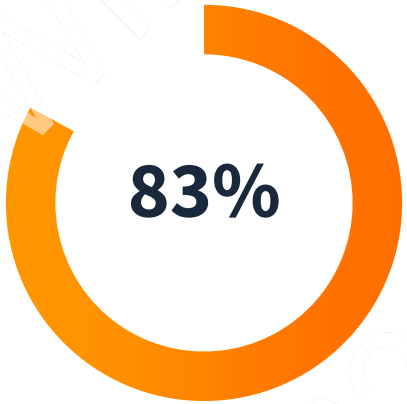
41-80 ODI
Severely disabled or crippled requirement



Mekhail N, et al. ECAP-controlled closed-loop versus open-loop SCS for the treatment of chronic pain: 36-month results of the EVOKE blinded randomized clinical trial. Reg Anesth Pain Med. 2023 Aug 27:rapm-2023-104751. doi: 10.1136/rapm-2023-104751

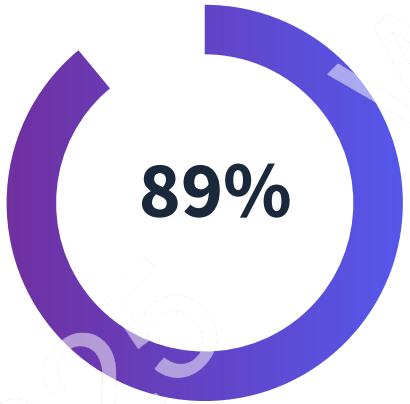
saluda MEDICAL

EVOKE Study Key Takeaways

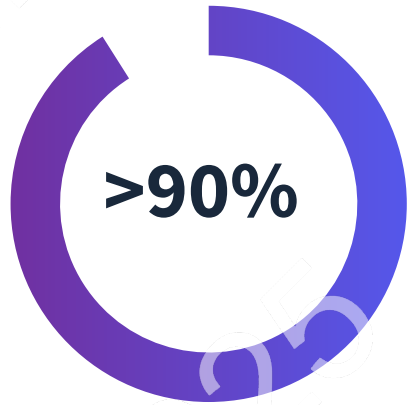


Pain Responders
(≥50% VAS Reduction)

High Pain Responders
(≥80% VAS Reduction)



of patients chose **SmartLoop® Therapy**



of responders at 3 months are **responders at 3 years**

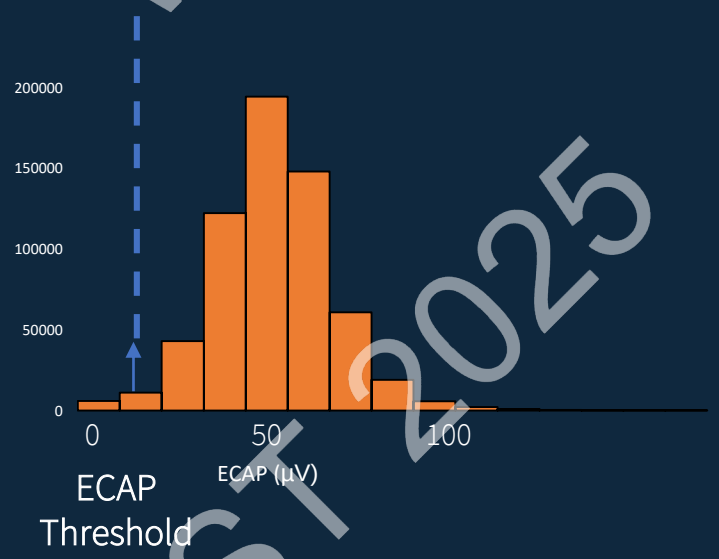
Mekhail NA, et al. Reg Anesth Pain Med 2024;0:1–8. doi:10.1136/rapm-2024-105370

saluda MEDICAL

Identification of Three Neural Metrics

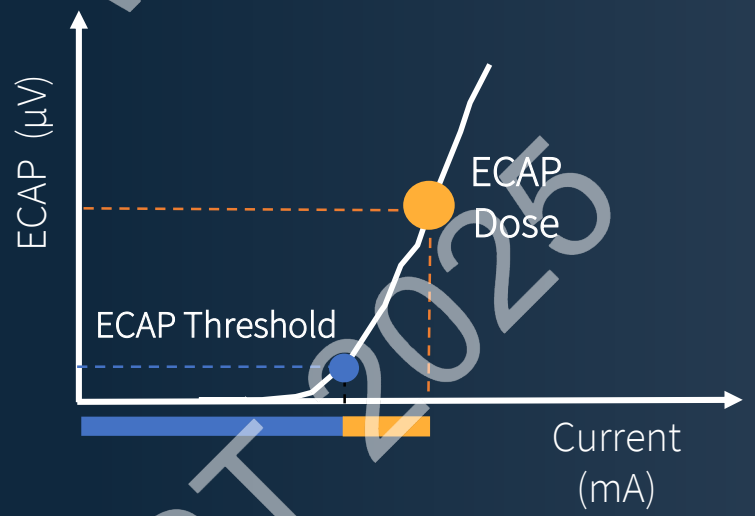
Is medication being taken?

1. Therapy Utilization



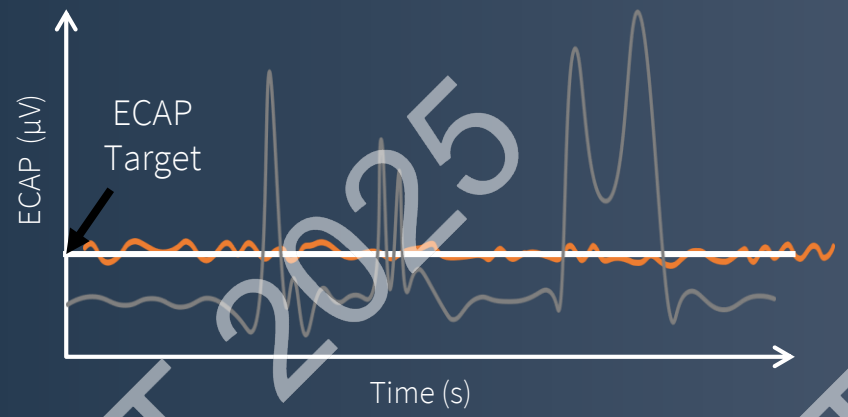
Is the dose optimized?

2. Dose Ratio



Is the dose taken accurately over time?

3. Dose Accuracy



saluda MEDICAL

Medtronic Inceptiv

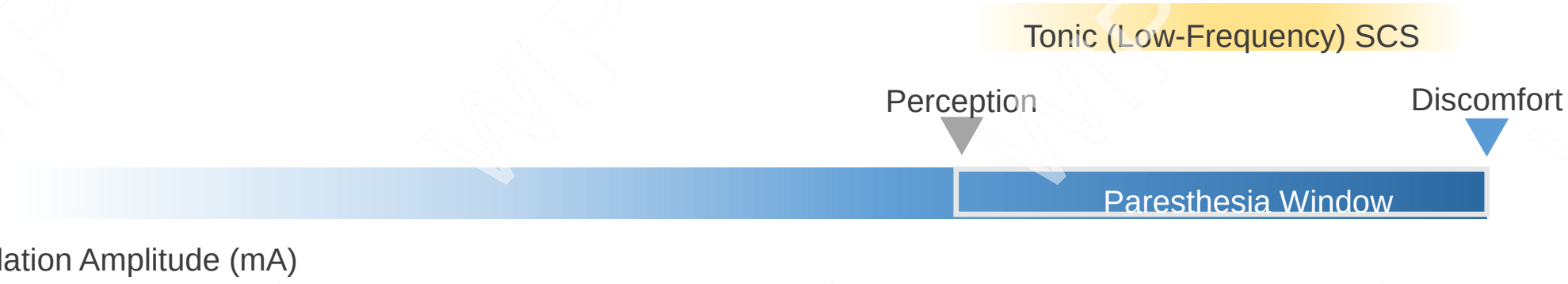
Inceptiv programming

- Two active channels
- ECAP generated via bipole at top or bottom of single lead
  - 50Hz at <200msc
- Second channel can provide a different therapeutic waveform
  - Supra or sub-perception
- But must use bipole on same lead

- We await robust outcome data in real world patients

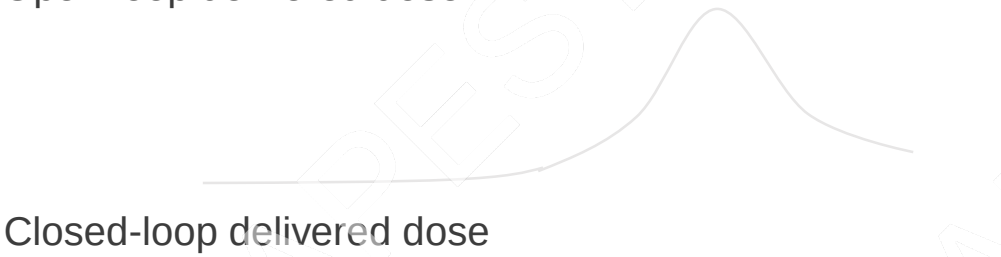
Automatic SCS dose control with ECAP sensing

- **Closed-loop SCS with paresthesia-centric therapy**



"ECAP Thermostat"

Adjust stimulation current to reduce or increase current once pre-specified upper and lower ECAP limits reached



Understanding sub-perception SCS

Supra versus Sub–perception SCS

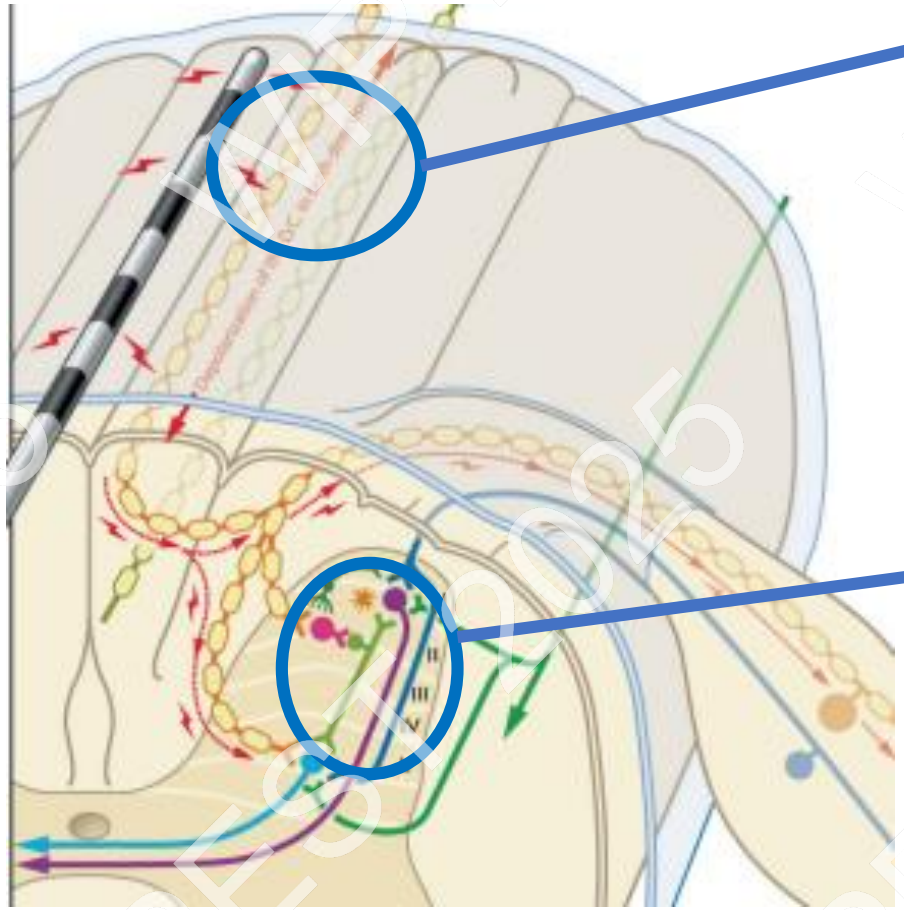
- Goal of supra-SCS is to maximise DC activation as observed by patient report of paresthesia pain area coverage
- Pain relief correlates with ECAP activation plot

- Biomarker = 1.2 to 1.6 – The Optimised Dose; above ECAP threshold

$$\frac{\text{Current at ECAP delivering best pain relief}}{\text{Current at ECAP Threshold}}$$

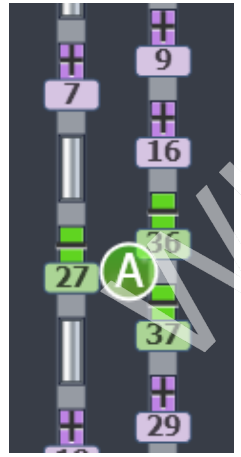
- SCS pain relief can be achieved without feeling paresthesia
- Sub-p SCS does not have a biomarker

What is the Neural Target(s) being activated?



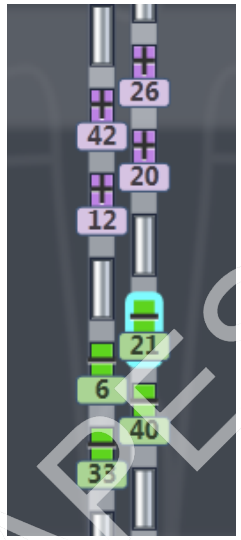
Super-Perception

- Target: ***Dorsal Columns***



Sub-Perception

- Target: ***Dorsal Horn Elements***



Sub-Perception SCS: Candidate Neural Targets

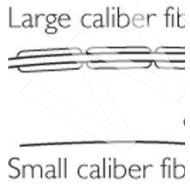
Proposed Hypotheses:

Root/A-Fiber Effects:
Liu et al. (2000)

Unmyelinated Effects: not likely:
Sikora, *IANS*, (2017)

Synaptic effects:
Li et al., *Neuromodulation*, (2018)

Other Targets:
Descending fibers.
Dorsal column collaterals.
Non-neuronal elements.
Etc…



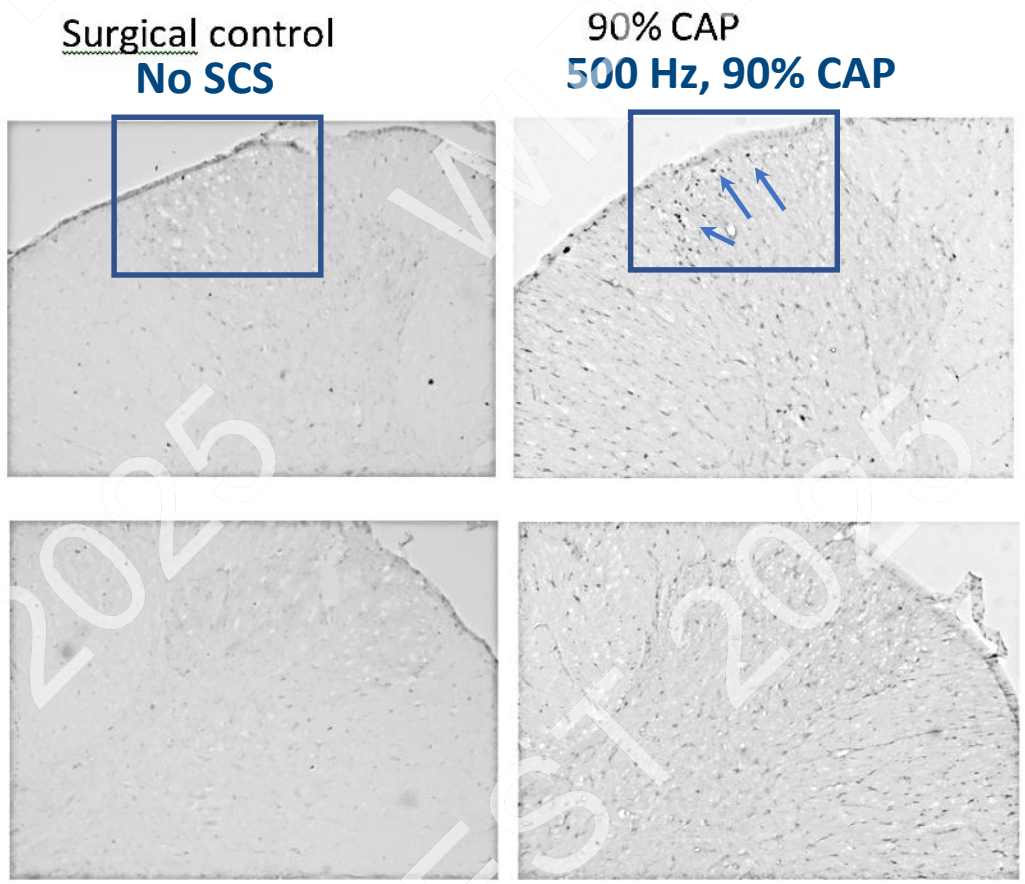
10X

Left

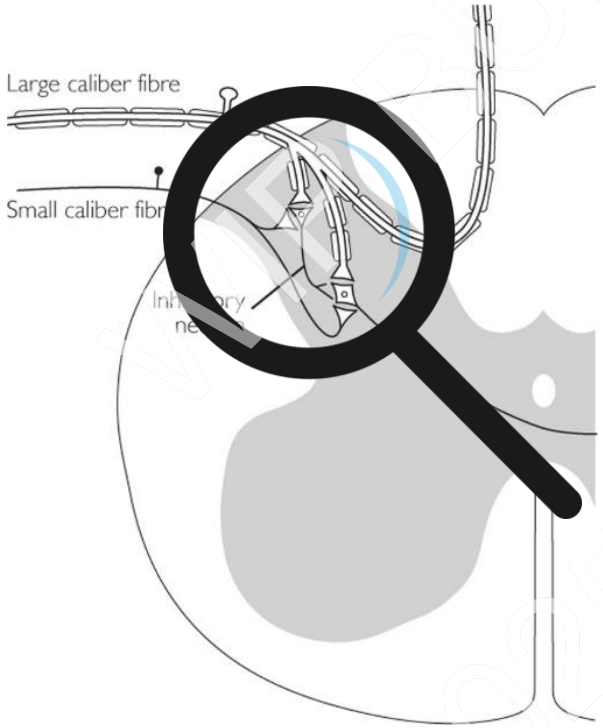
SCS Ipsi.

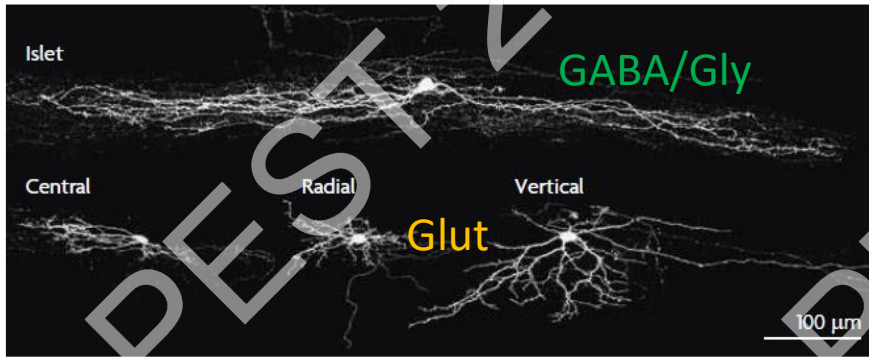
Right

SCS Contra.



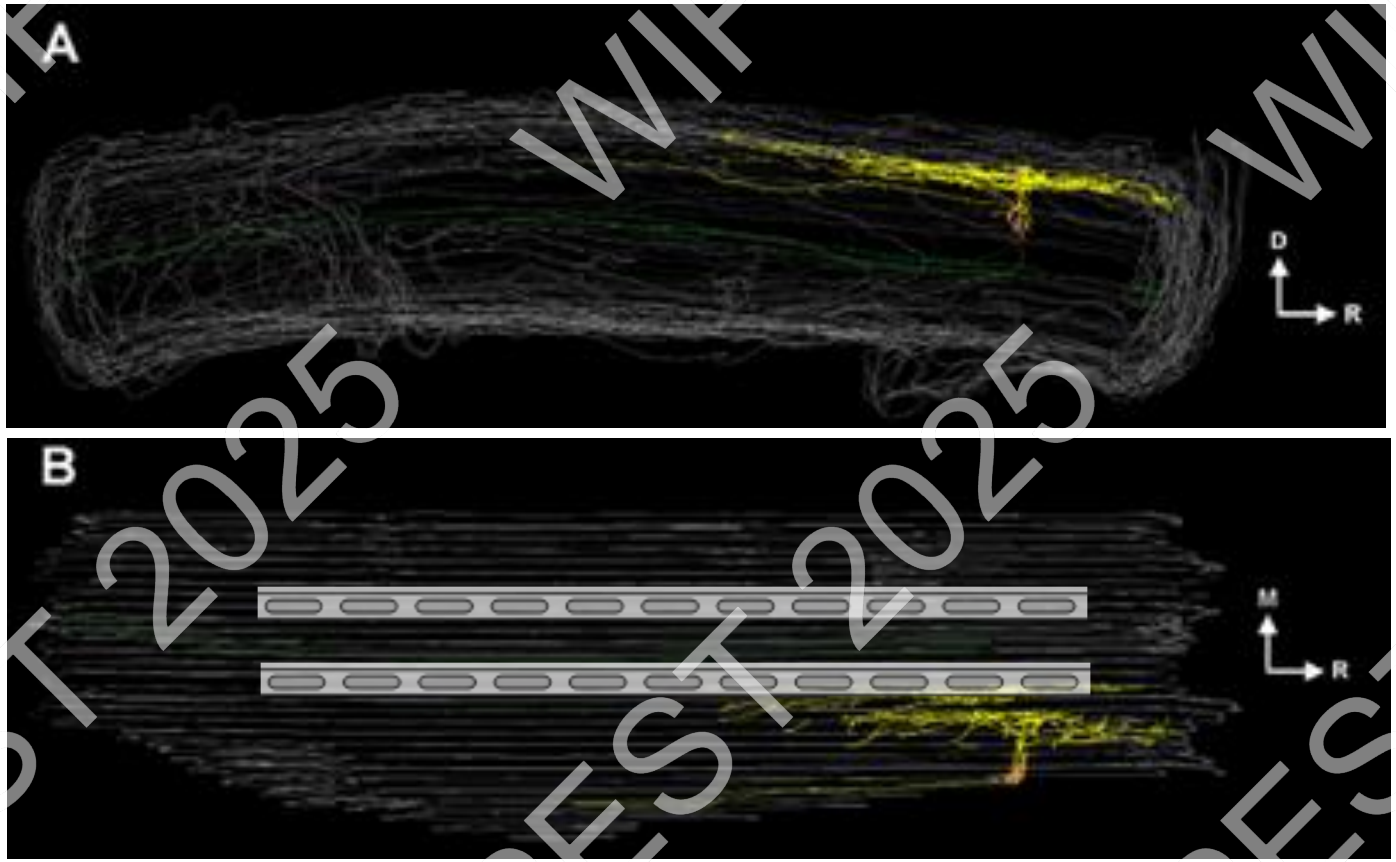
Sub-P Modeled Target: Dorsal Horn interneurons





Todd, *Nat. Rev.* 2010

Synaptic terminals of superficial dorsal horn with rostrocaudal orientation



Szucs et al., J Comp, 2013

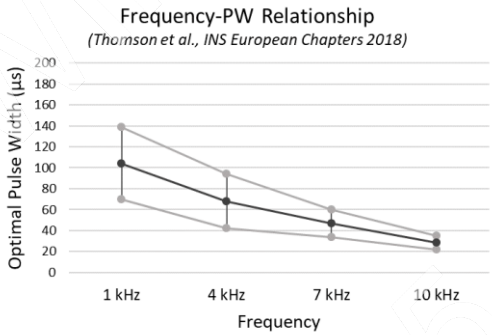
The Neural Dosing (sub-p) work (2014-2021)

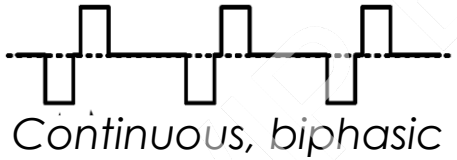
Waveform = f(amplitude, pulse width, frequency)

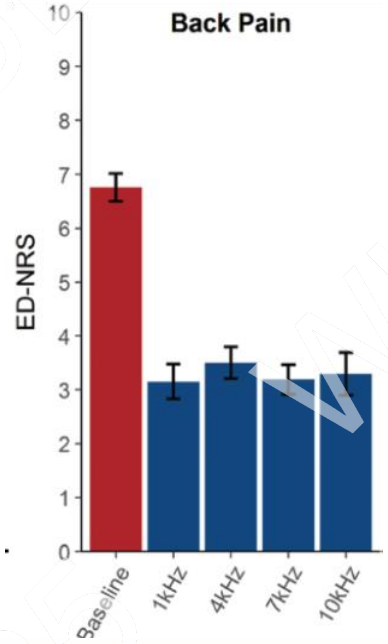
PROCO RCT

[Thomson et al., 2018]

@ 10, 7, 4 and 1 kHz



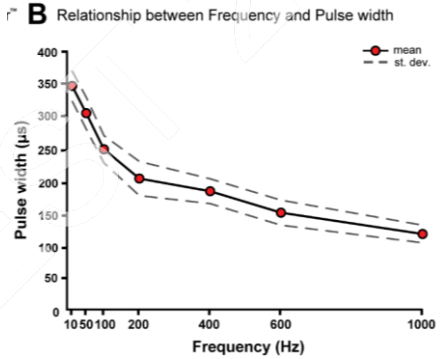


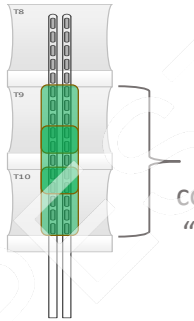


HALO Study

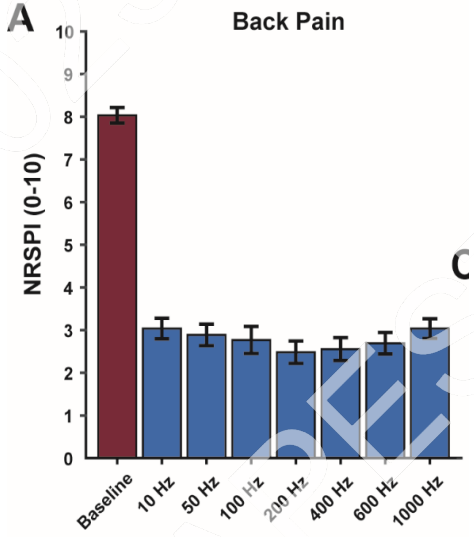
[Paz, Thomson et al., 2021]

@ 1 kHz, 600, 400, 200, 100, 50 and 10 Hz



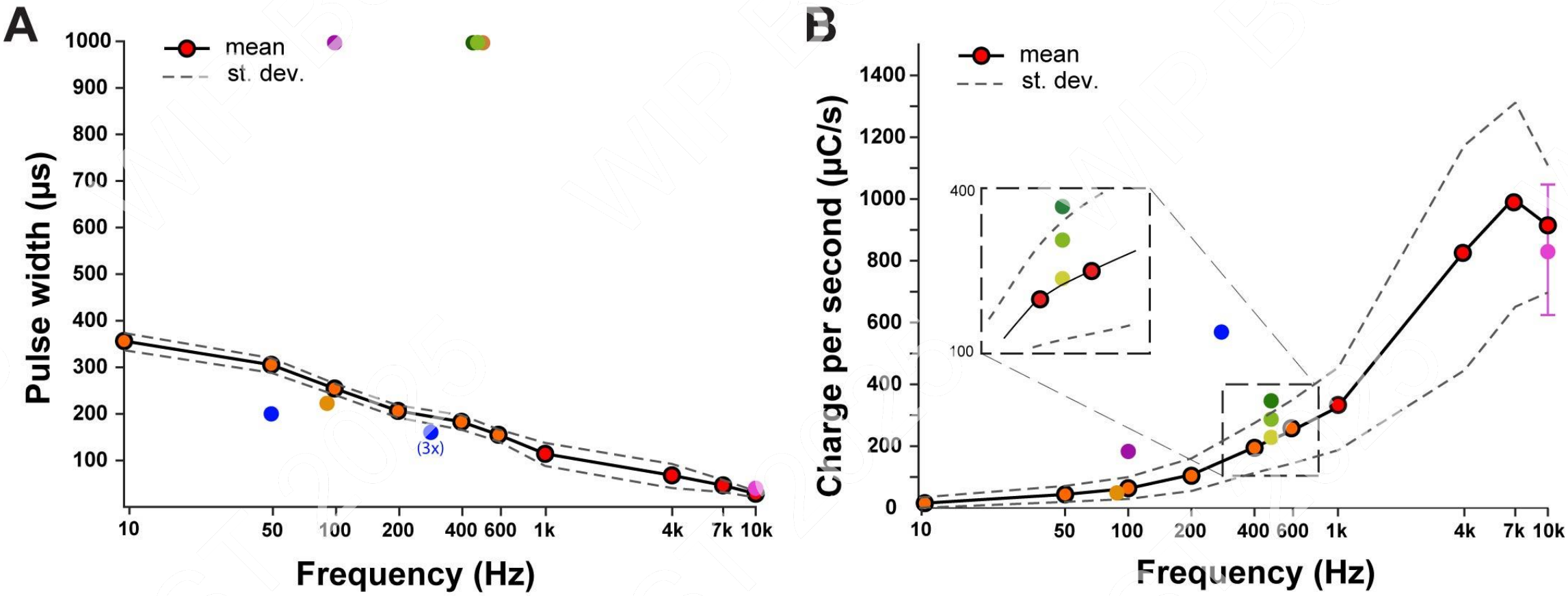


Broad field covers multiple "sweet spots"



The Neural Dosing plot

Any waveform could be mapped onto our neural dosing plot with high-school maths.



Neural Dosing:
Thomson et al., 2018
Paz & Thomson et al., 2021

BurstDR:
Deer et al., 2017
Tavel et al., 2017
Vesper et al., 2019

Subwave:
Russo et al., 2023

Fast-Acting (FAST):
Metzger et al., 2021

Differential Time Multiplex (DTM):
White et al., 2024

High Frequency (10 kHz):
Kapural et al., 2015

Therapeutic window in High-Charge space

High Charge stimulation patterns constrain the therapeutic window

HF10 *0.1 x 30 x 10,000 =* ***30 µC/s***

BurstDR *0.1 x 5 x 1000 x 40 =* ***20 µC/s***

DTM *0.1 x (3 x 170 x 300 + 200 x 50)=* ***16.3 µC/s***

Subwave *0.1 x 1000 x 100 =* ***10 µC/s***

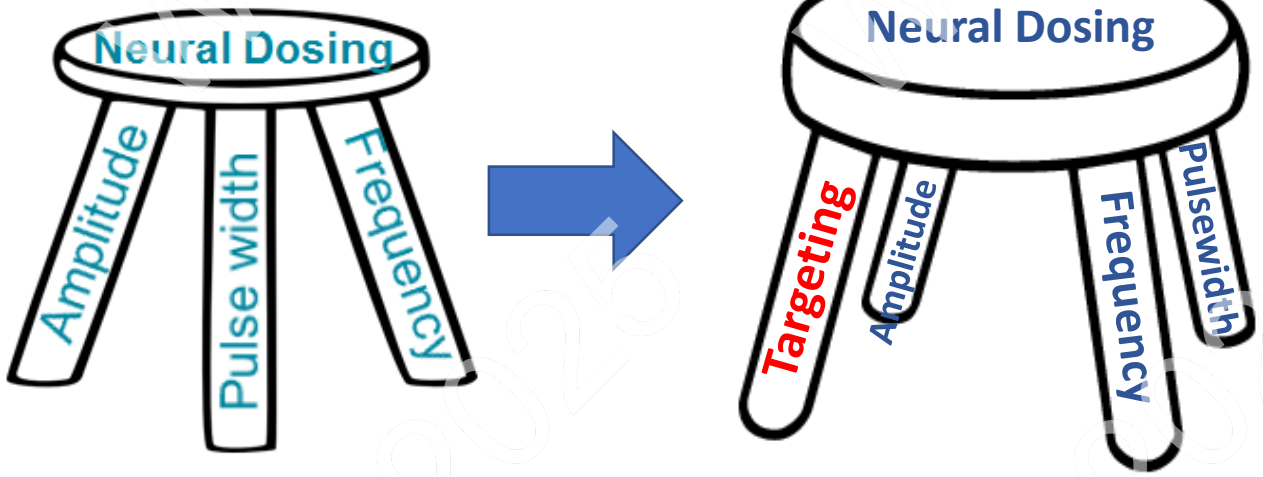
FAST *0.1 x 230 x 90 =* ***2.1 µC/s***

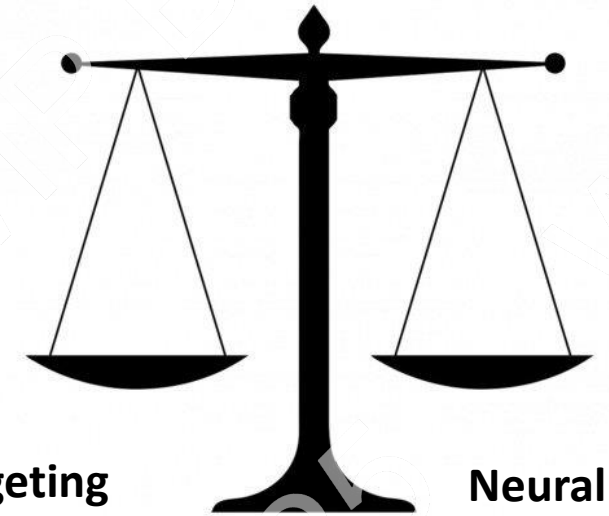
A 0.1 mA amplitude increase (RC or small movement) has a huge effect on charge

→ ***500-1400%*** *more Charge per Second for every 0.1mA change !!*

* Duty cycling would minimize this impact

Is this still enough for SCS success?





Targeting

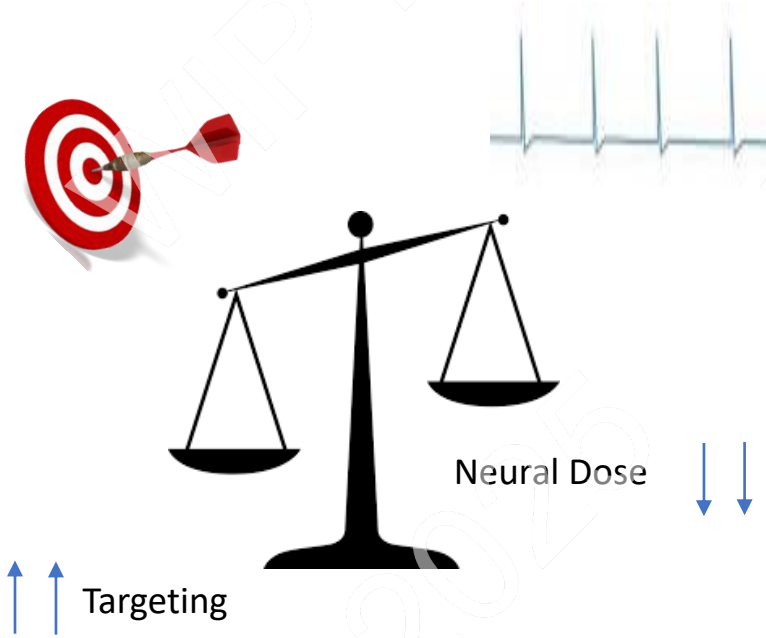
Lead placement
Contact spacing
IPG technology

Neural Dose

Charge delivery at most efficient settings

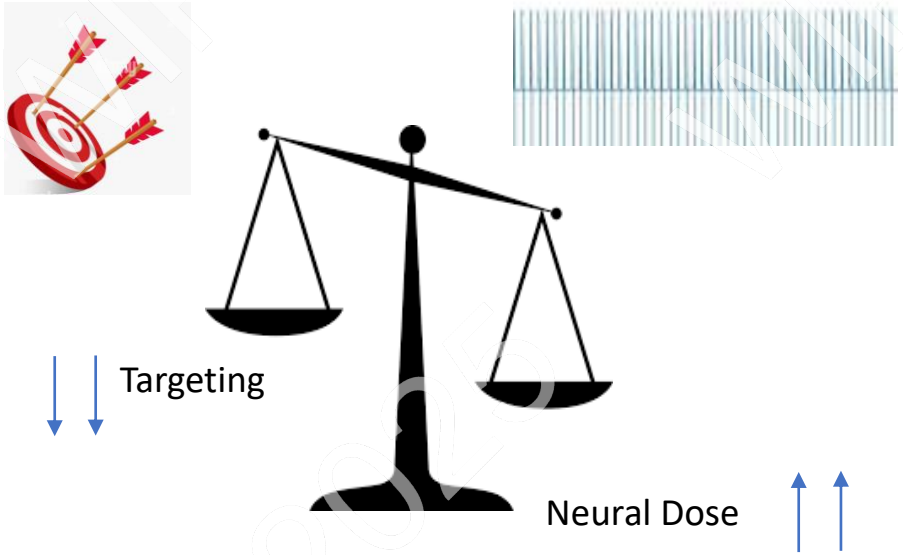
Hypothesis: Targeting vs. Dose tradeoff

When targeting is precise, low dose can be afforded



- **Paresthesia-guided**
- **Low Frequencies 50-100Hz**

When targeting is NOT precise, high dose is required



- **Anatomical-guided (blind)**
- **kHz therapy**

Problems with fixed output SCS

Paresthesia SCS – Open Loop

- At maximum DC activation, VTA variation can be uncomfortable
- Stimulating current is manually reduced to avoid such events
- DC activation is reduced
- Pain relief and pain areas are reduced
- Sub-optimal pain relief

Sub-perception SCS

- Modes that rely on high charge delivery and/or poorly targeted
  - Small therapeutic window
- Under-stimulation
  - Sub-optimal pain relief
- Over-stimulation can result in
  - Sub-optimal pain relief
  - Symptoms of over-stimulation
  - Therapy Habituation

Fixed output SCS in sub-perception

Low charge, targeted sub-p SCS modes

- Limited effect on outcome with change in amplitude caused by movement
- Larger therapeutic window for sub-p SCS
- Pain relief sustained

Other solutions

- Use ECAP measurement at near threshold SCS
- If recorded ECAP is above pre-set level, the sub-p amplitude is automatically reduced before gradually restored
- Prevents over-stimulation

Medtronic Inceptiv

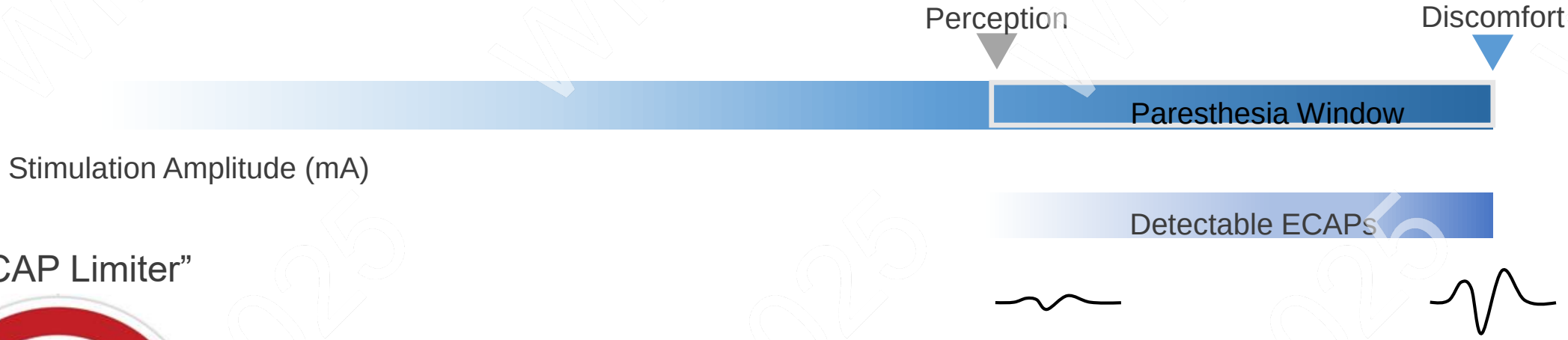
Use of ECAP in sub-perception programming

Automatic SCS dose control with ECAP sensing

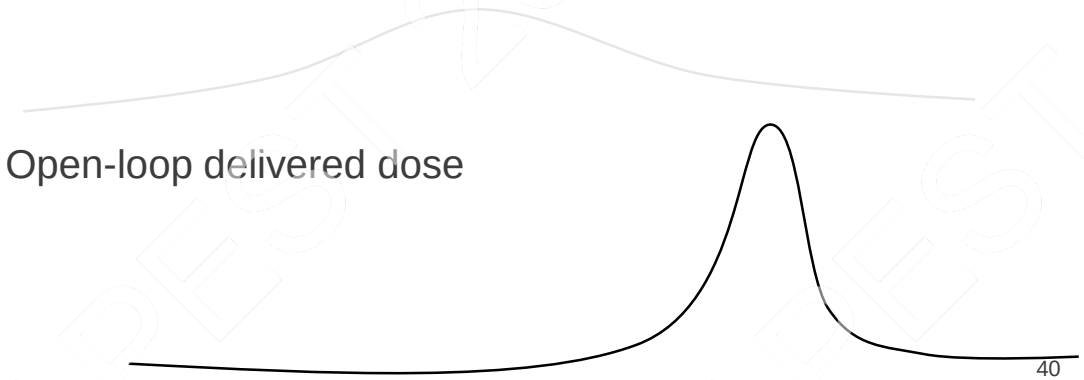
- **Closed-loop SCS with therapy at or near perception**

Modern SCS

Sub-perception, bursted, etc…

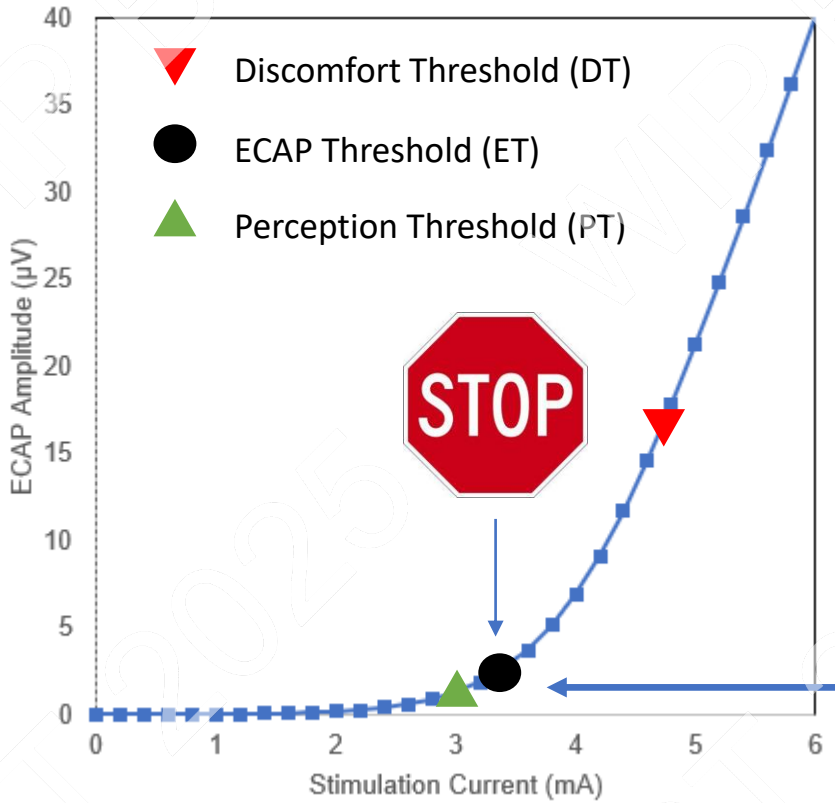


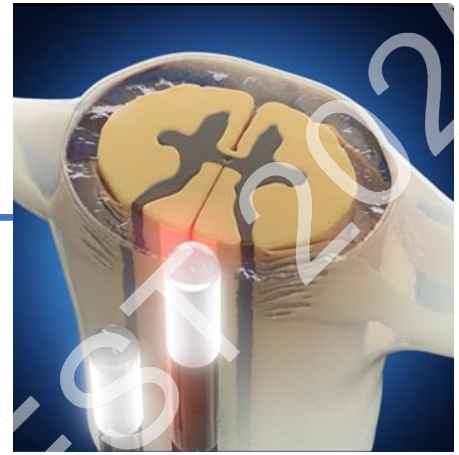
"ECAP Limiter"



Automatic SCS dose control with ECAP sensing

- **Closed-loop SCS with therapy at or near perception**





3 µV at 3.2 mA

Automatic SCS dose control with ECAP sensing

Conclusions

- SCS continues to evolve
- Developers seek ways of providing optimized patient centric outcomes
- ECAP measurement allows objective measures of dorsal column activation
- Closed loop allows automatic adjustments
- Supra perception SCS is required for ECAP generation
- Maximal pain relief is achieved at optimum neural dose & accuracy
- Sub-perception SCS ECAP’s can be detected at near threshold and indicate over-stimulation allowing for power reduction and ramp up

Conclusions

- Is there an ARMS RACE?
- The two commercial products are not the same
- Closed loop is a game changer for Supra Perception Parasthesia SCS

- Value of Closed loop in Sub-perception
- Still to be determined
- Depends upon the neural dose and targeting
- High versus low energy sub-perception SCS

Thanks for Listening

www.drsimonthomson.com