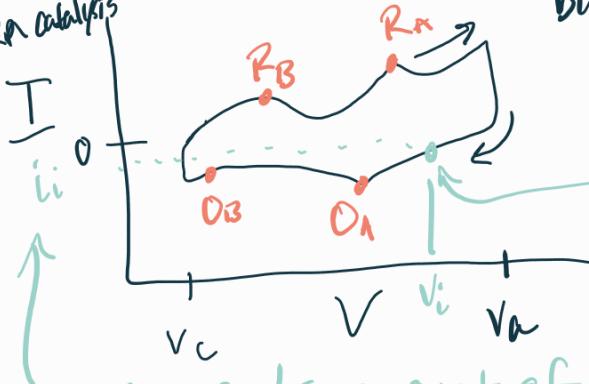
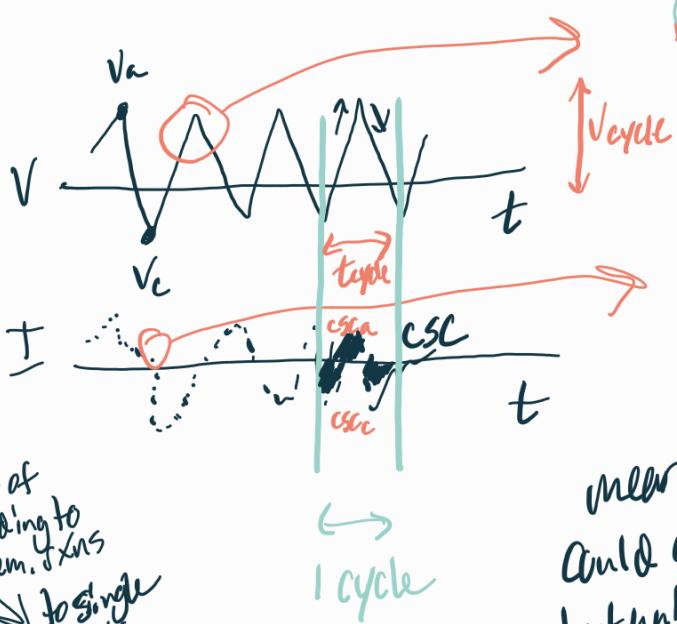


Application ← → Measurement Standards

- Category Basis?
- Time (<sup>Freq.</sup>  
Pulsewidth)
- Options for Manipulating Neural Activity
  - Chemical
  - Electrical
  - Signaling/Transmitters
- Needs?
  - Q<sub>inj</sub> Limit
  - "Safe" Waveforms  
(When Will Tissue Damage Occur?)

# Cyclic Voltammetry



represents amount of species C oxidized while electrode material is reduced when potential is at  $V_{ref} + V_i$



exact  $i$  value depends on ↓ sampling strategy

fast scan rate  
slow scan rate

$$\Delta t_i$$

means many species and contribute to Q movement in vivo but unknown how much, in what way/etc.

scan rate

$$r = \frac{V_{cycle}}{t_{cycle}} = \frac{\Delta V_{step}}{\Delta t_{step}}$$

\* Only measures rxns w/ species present inside the cell! Not in all, no measure of Q contribution

↑ define electrochemical potential!

CSC ← comes from battery research; equivalent to (?)

at slow scan rate, represents total amount of charge material

↑ define "slow" could potentially move # of molecules of

Charged Species (A, B, C, other) it can oxidize (CSC<sub>c</sub>) and reduce (CSC<sub>a</sub>) within the voltage window [V<sub>c</sub> to V<sub>a</sub> vs. V<sub>ref</sub>] tested.

Time scale ( $\Delta t_i$ ) for 10mV step, 50mV/s CV = 0.2s = 200ms

Time scales of neuromodulation current pulses = 2ms or less when polarized over the entire water window voltage range.

If electrode is not polarized w/in voltage range during neuromodulation, it cannot catalyze rxns that require that potential difference (vs. V<sub>ref</sub>) to occur → therefore, material will not be able to utilize those rxns for for Q delivery, effectively lowering applicable CSC value/quantity.

Paper: "Stop using cyclic voltammetry to decide what electrode material is better for neuromodulation"

## CV Utility: • validate material integrity / composition

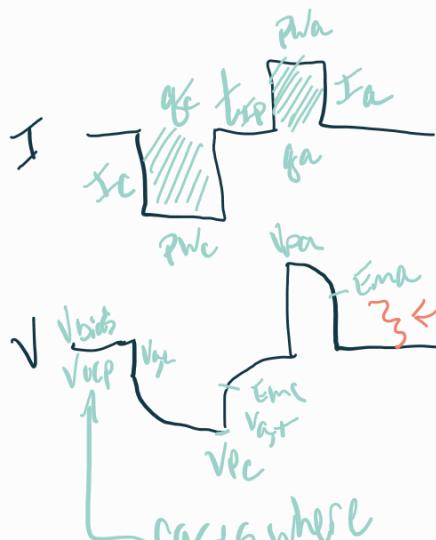
- Not CSL #, SHAPE of CV curve! = value ↴
- manufacturing quality control metric
- interrogate Q transfer processes & redox rxns @ interface
  - ↳ investigate degree of involvement of particular ionic species in Q transfer

- ↑ CSC will translate to ↑ Qinj for some materials. But ↑ CSC will not always translate to ↑ Qinj for all materials.
- If you want to determine what material provides a higher Qinj (wider operating range for delivering therapy), measure changes in/differences in Qinj w/ shortest & longest PW used in your application.

Default if PW range unknown can be 50us and 500us. [need to support # choices]  
 NOTE importance of hardware selection & waveform settings!

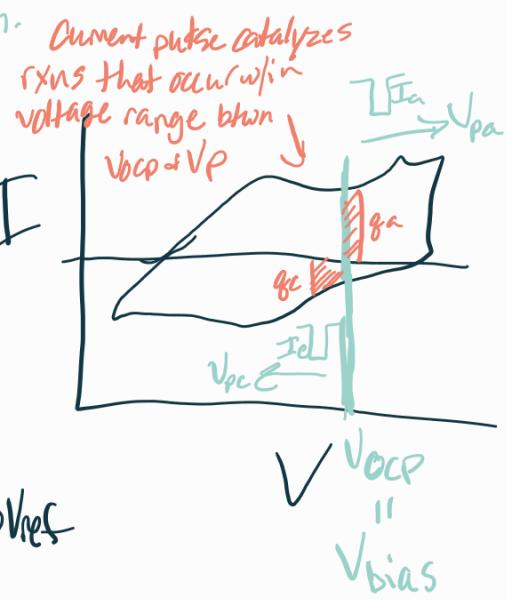
Designing materials for high CSC is designing electrodes to perform well on a task that is not the same as task performed in neuromodulation.

## VT



Explain Overpotentials  
in PBS vs in vivo

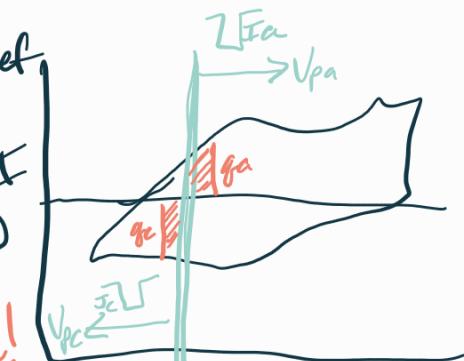
If  $V_{OCP}$  of material is  $\oplus V_{ref}$



CASES where  
 $V_{OCP} = V_{bias}$   
 $V_{OCP} < V_{bias}$   
 $V_{OCP} > V_{bias}$

If  $V_{OCP}$  of material is  $\ominus V_{ref}$

Changes this relationship



\* Influence & Importance of Reference Electrode!

If ref for VT ≠ ref for CV

Cannot directly relate VT Voltage values to CV voltage values

need to adjust by  $\Delta(V_{ref} - V_{CV})$  ← if  $V_{ref}$  is in vivo or non-standard

thermodynamically stable ref electrode, becomes very difficult to know

relationship btwn  $V_{ref}$  &  $V_{CV}$ , & therefore difficult to estimate what rxns are occurring during the I pulse (in addition to unknown/uncharacterized baseline likely rxns btwn electrode material & molecules/species present in vivo, not in PBS)

\* Influence & Importance of Hardware Components! See Alexander Hiri's paper.

## Utility of VT

- Metrics for expected neuromodulation performance
- Interrogate material's utility for intended use/application
- Waveform (therapy) Development: quantify pattern's effect on electrode material
  - ◇ stays w/in Vc-Va range?
  - ◇ fluctuations over time?
  - ◇ does pulsing near limit of material's Q<sub>inj</sub> limit induce stress/structural change? over time?
    - ← Q<sub>recovery</sub>
    - ← Explain thermodynamic limits (diffusion) w/ scenarios where likely high influence vs low influence
- ◇ Time/Duration limitations for Q movement w/in each phase of I pulse
  - \* Including IP Delay + control method!
  - \* Including inter-pulse period + control method!

## Reasons to do VT in PBS vs. in Vivo!

- Situations where PBS may be more aggressive → foreseeable material effect of electrolyte conductivity on 'stress' of Q movement?
- Situations where in Vivo may be more aggressive capacative vs. faradaic Q-transfer: materials & redox rxns
- ⑧ Different materials will be better-or-worse-suited to different pulsing strategies for therapeutic charge delivery.
- VT can assist in screening: what material, what geometry/geom., what surface topography, what surface area? is likely to successfully & [and what combinations/ranges of each/all factors] reliably deliver your neuromodulation therapy

- ④ Shortcuts to not test across entire range of PW/freq. Combinations
- ① set IP delay for what you want @ electrode btwn pulses
    - thermodynamic-driven [not controlled] "recovery" → no delay, immediate controlled Q reversal
    - controlled discharge, short to counter
  - ② Test @ ends of potential therapeutic ranges w/ most expected amplitude
- |              | PW ↓  | freq ↑ | Q recovery btwn pulses | Q <sub>total</sub> + Q <sub>density</sub> | Q density : Time |
|--------------|-------|--------|------------------------|---|------------------|
| most stress  | IPW ↑ | freq ↑ | most challenging       | ↑ PW most                                 | ↓ PW Most        |
| least stress | IPW ↓ | freq ↓ | least challenging      | ↓ PW Least                                | ↑ PW Least       |

## EIS

1 kHz  $|Z|$  magnitude useful + easy/quick to measure  
indicator of electrode (recording channel; including electrode site +  
wire/trace + connector + pins) integrity  $\rightarrow$  proxy for ability to record neural activity/

- range of neuron firing rates; dependence on cell type, physiological signal
- behavior and frequency dependence of different materials
- utilize material properties to target recording cell types of interest?
  - $\rightarrow$  use material R vs. C behavior in firing rate freq. range to select electrode
  - $\rightarrow$  don't forget influence of GSA on EIS values

## Utility of EIS

in PBS :

in vivo :

electrode-tissue

- Interrogate properties of electrode-electrolyte interface.
  - $\rightarrow$  comment on 4-electrode experimental set-ups + reported data
  - $\rightarrow$  suggest additional experiments that can answer questions applicable to moving many parts of the neuromod field forward

## Cross Talk / Leakage Current Measurements

- Traces: size + spacing/pitch
- Current Amplitude
- Frequency

# Other / New Measurements For Neurotechnology

I steps?

V steps?

Benchtop?

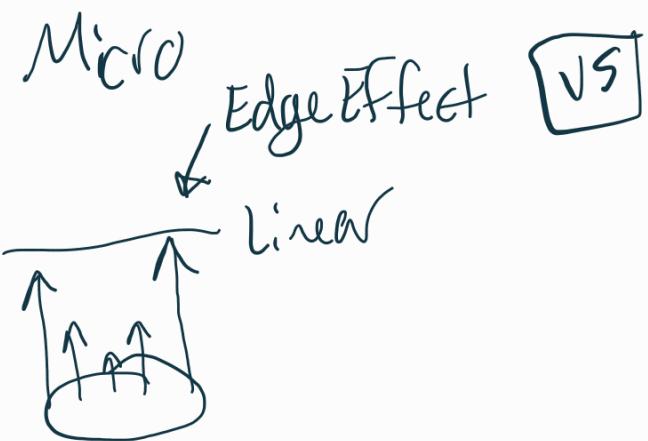
VS

In Vivo?

Needs For  
Each?

- ④ Discuss:
- ① Zeng & Huang (2023) 10.1002/adfm.202301223
  - ② Schiafone et al. (2020) 10.1016/j.neuron.2020.10.010
  - ③ Yi, Yao, Wang, Chen (2022) 10.1115/1.4063179

2D Disc



Ultra Micro



Calculate Concentration O<sub>2</sub> or H<sub>2</sub> generated  
on microelectrode w/ sustained redox of H<sub>2</sub>O  
→ relate to concentration [M] in tissue overall  
→ time scale of natural bicarbonate buffering