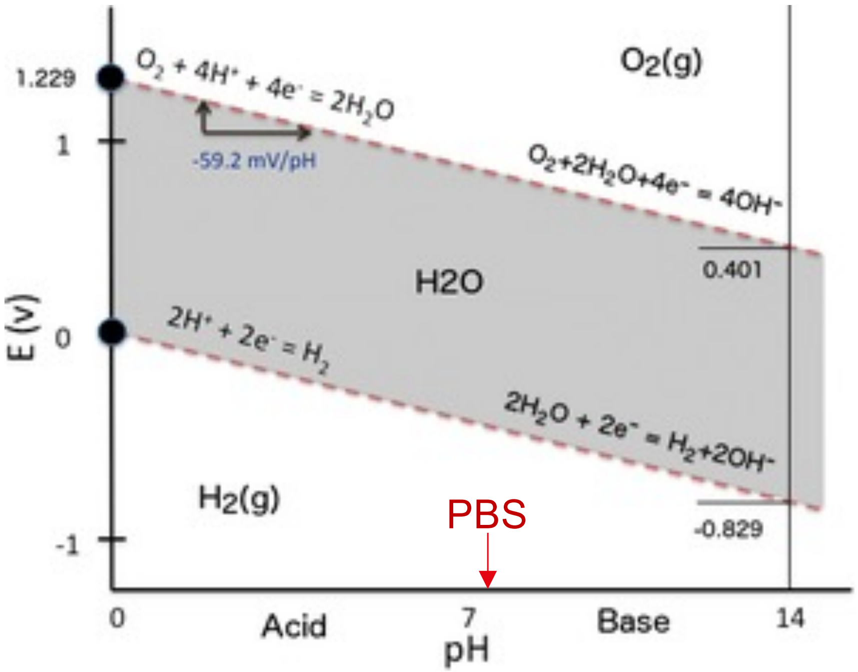
Neural stimulation neuromodulation

- Current flowing between 2 electrodes will
  stimulate the tissue at the **cathode** (negative electrode)
  resist excitation at the anode (positive electrode)

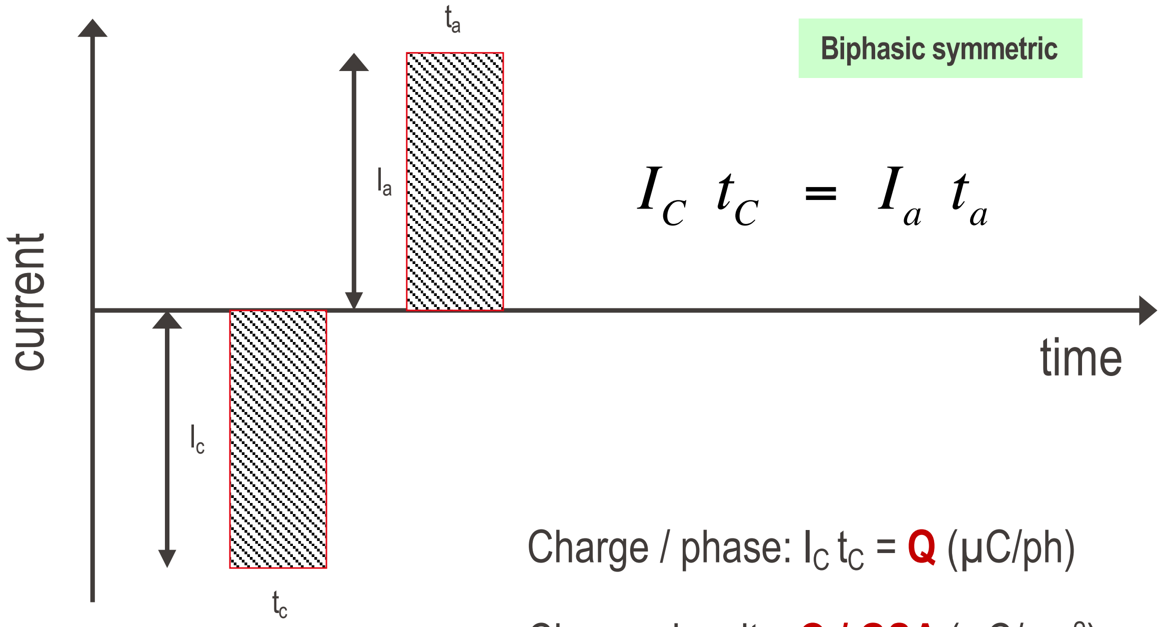
- Cathodic stimulation: depolarization of the cell membrane i.e. generation of an action potential

The water window

- Electrochemical window within which the electrode material is neither oxidized nor reduced.
- The electrolyte, the solvent and the nature of the working electrode influence the potential window
- Water electrolysis requires 1.23V (potential across 2 inert electrodes)
  - -0.6V - +0.8V



Constant current pulses



Biphasic symmetric

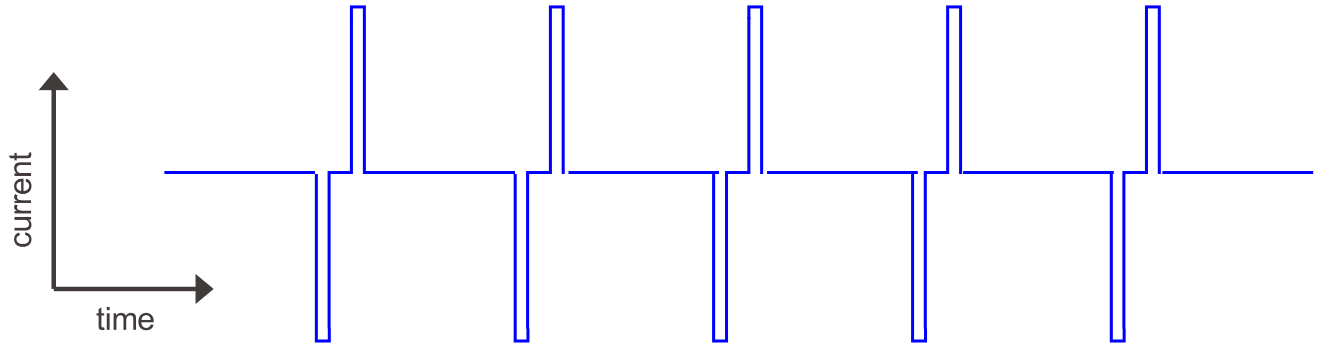
$$I_C \; t_C = I_a \; t_a$$

Charge / phase: $I_C\, t_C$ = **Q** (µC/ph)

Charge density: **Q / GSA** (µC/cm²)

Neural stimulation

- Applying a train of current pulses to the target tissue



Challenge: produce reversible charge-injection chronically

Reversible = { no electrode damage (corrosion)
no tissue damage

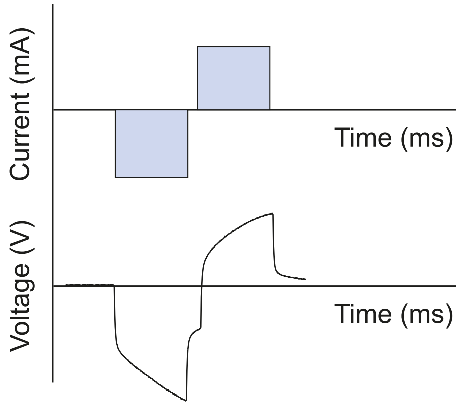
Voltage transient measurements

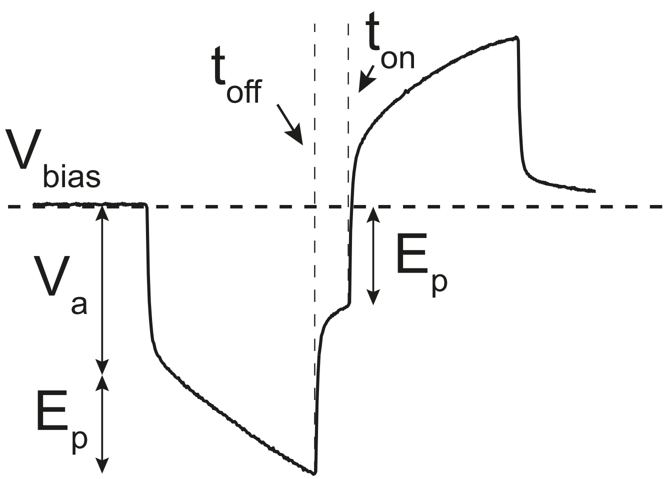
- Estimate the maximum charge that can be injected in a current-controlled stimulation pulse
- 3-electrode setup (in vitro)
  - Determine maximum polarization (most negative and positive potentials)
  - Safe boundaries: water window and reduction potentials

$$\Delta V = i_c R_i + \eta_c + \eta_a + \Delta E_0$$

R_i	electrolyte resistance
η_c	concentration overpotential
η_a	activation overpotential
ΔE_0	shift in the equilibrium potential

Voltage transient in response to a biphasic current pulse





- V_{bias}: equilibrium potential (half-cell potential)
- V_a: Access voltage (ohmic drops)
  - IR drop in the interconnect
  - IR drop in the tissue/electrolyte
  - Concentration overpotential
- E_p: Electrode polarisation at the interface
  - Activation overpotential
  - Potential equilibrium shift
- **E_{min}: Minimum cathodic polarization = $V_a + E_p$**

$$E_{min} = IR + \eta_c + E_o + \eta_a$$

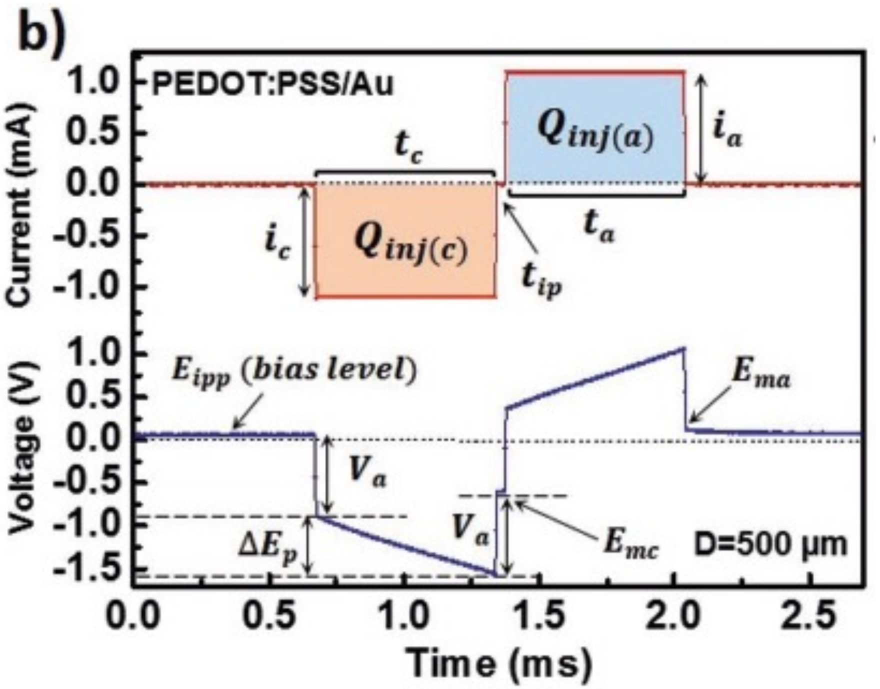
V_a — Around the electrode

E_p — At the interface

Charge Injection Capacity CIC

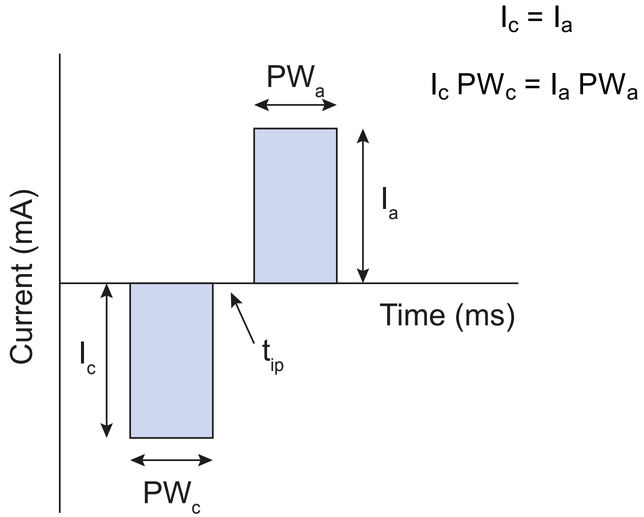
- **E_{mc}**:
  - maximum cathodal electrochemical potential excursions calculated by subtracting V_a from the maximum negative voltage transients or the electrode potential immediately, (when V_a is zero)
- **E_{ma}**:
  - maximum anodic electrochemical potential excursions
- Injected charges: $\mathbf{Q_{inj} = Q_{inj(b)} + Q_{inj(a)}}$
- **CIC**:
  - total charge density at which either E_{mc} reaches water reduction potential (cathodal limit) and/or E_{ma} reaches water oxidation potential (anodal limit).

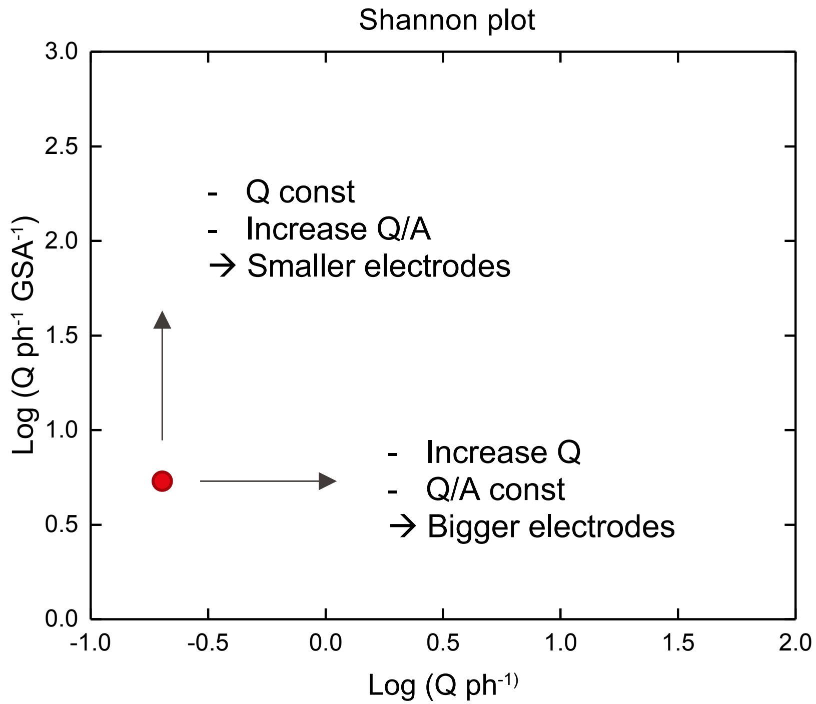
$CIC = Q_{inj,c} / GSA$



Shannon Plot

Biphasic, cathodic leading, charge balanced, symmetric pulses





When discussing safety and often for ease of comparison:

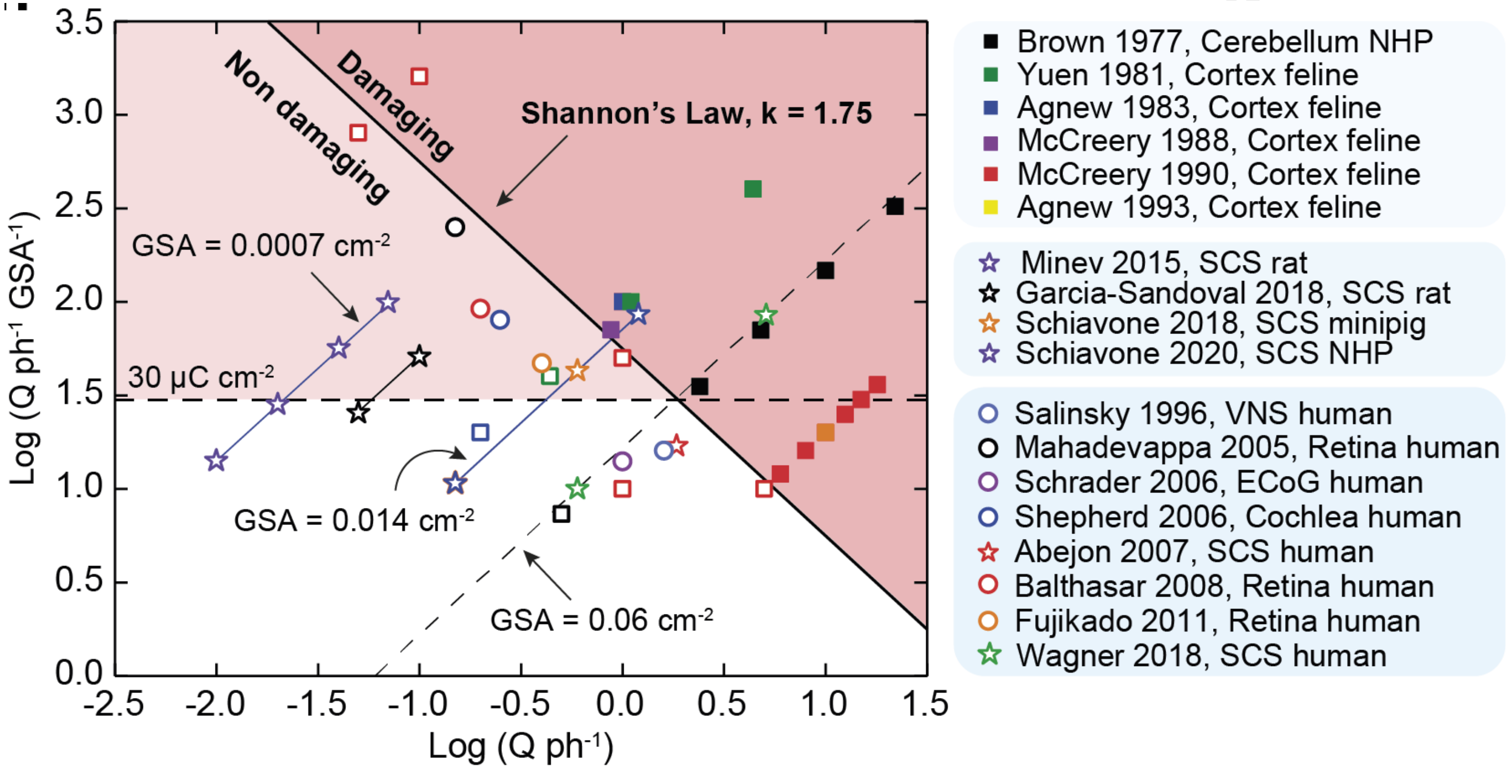
- $Q/ph. = I_c PW_c$ [μC ph^{-1}]
- Q/GSA = Q/ph./GSA [μC ph^{-1} cm^{-2}]

effect of electrode size

Charge vs charge density for safe stimulation

"the Shannon limit" $\log\left(\frac{Q}{A}\right) = k - \log(Q)$

1.5<k<2

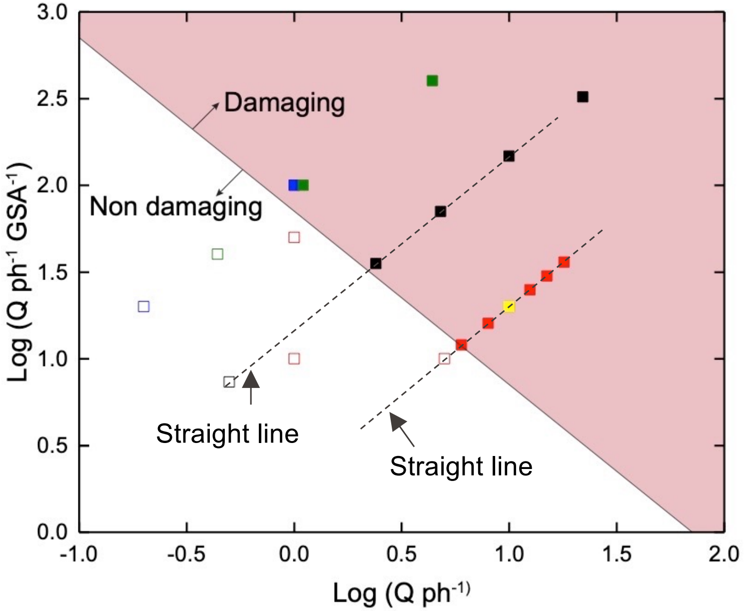


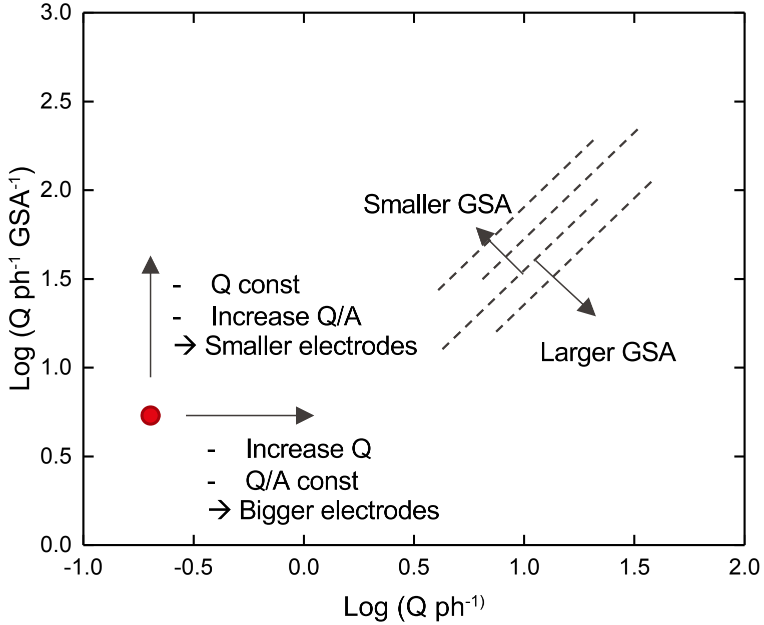
UNSAFE: irreversible electrochemical reaction
tissue damage
neuronal hyperactivity

Geometric surface area GSA on Shannon plot

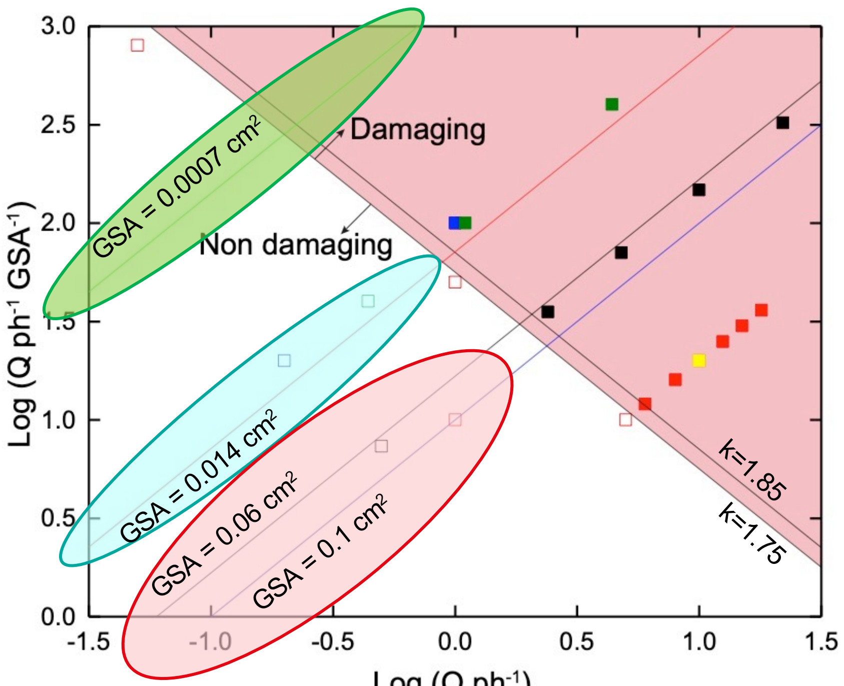
"the Shannon limit" $\log\left(\frac{Q}{A}\right) = k - \log(Q)$

"geometry" Log (Q/A) = Log (Q/ph) – Log (A);





The 30 μC.cm⁻² limit



MACRO / CLINICAL: e.g. SCS, DBS, VNS

MESO: e.g. e-dura (Pt composite) in minipig, NHP

MICRO: e.g. e-dura (Pt composite) in rat

For Medtronic SCS / DBS: GSA = 0.06 cm^2

→Log (Q/A) = Log (Q/ph) – Log (0.06);
Log (Q/A) = k – Log (Q/ph);

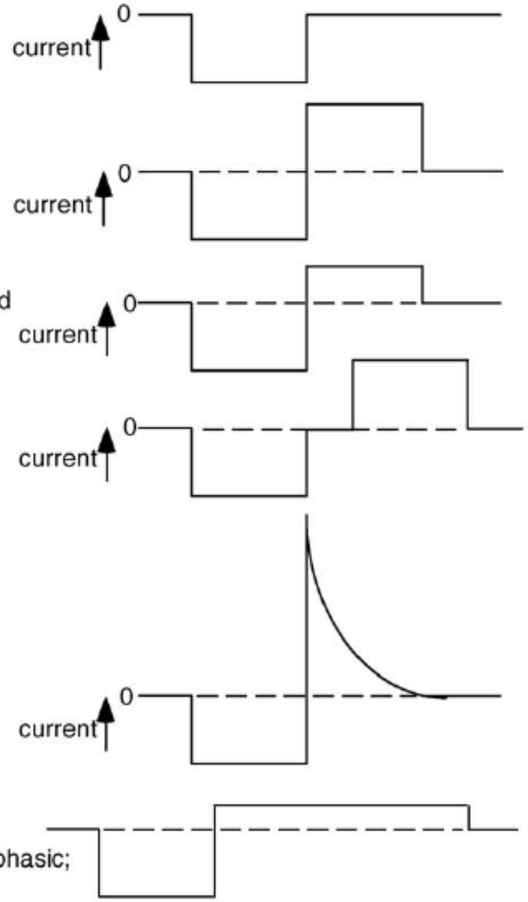
For k = 1.75:

→Log (Q/A) = 0.5 (1.75 – Log (0.06)) = 1.486;

→Q/A = $10^{1.486}$ ~ 30 μC cm^{-2}

Stimulation waveforms

Journal of Neuroscience Methods 141 (2005) 171–198



Waveform	efficacious AP initiation	tissue damage	corrosion
(a) monophasic	+ + +	- - -	+ + +
(b) charge balanced biphasic	-	+ +	-
(c) charge imbalanced biphasic	+	+	+ +
(d) charge balanced biphasic with delay	+ +	+	-
(e) charge balanced biphasic; fast reversal	- - -	+ + +	-
(f) charge balanced biphasic; slow reversal	+ +	- -	+

Electrochemical and biological safety in neural stimulation

- For different materials, geometries and pulses, the CIC limits vary widely
- CIC does not scale linearly with electrode area, but with electrode perimeter
- **Macroelectrodes** (GSA > $1 cm^2$)
  - $Q_{inj} < 50\ \mu C / cm^2$

Platinum

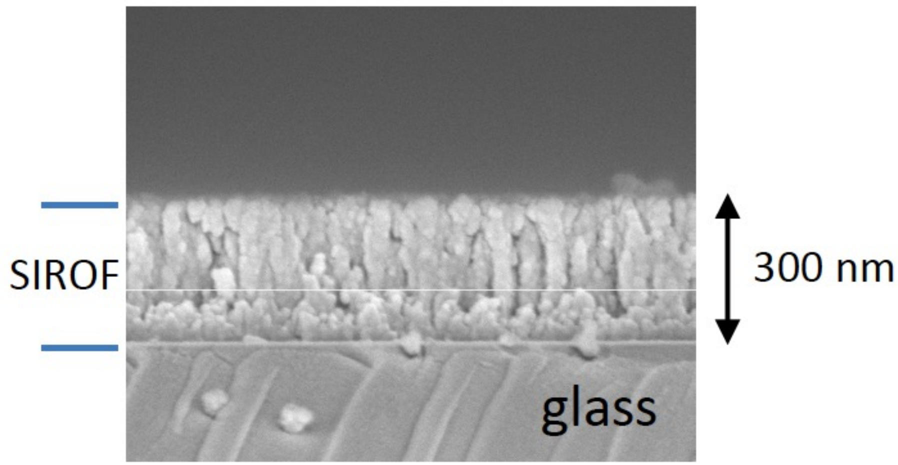
- « pseudo-capacitive » interface (surface redox process)

- Modest charge-injection capacity: < 100µC / cm^2
- « the » clinical electrode material

Iridium oxide

- Most charge injection is by redox processes
- Fabrication
  - Electrodeposition
  - Sputtering
  - Thermal deposition

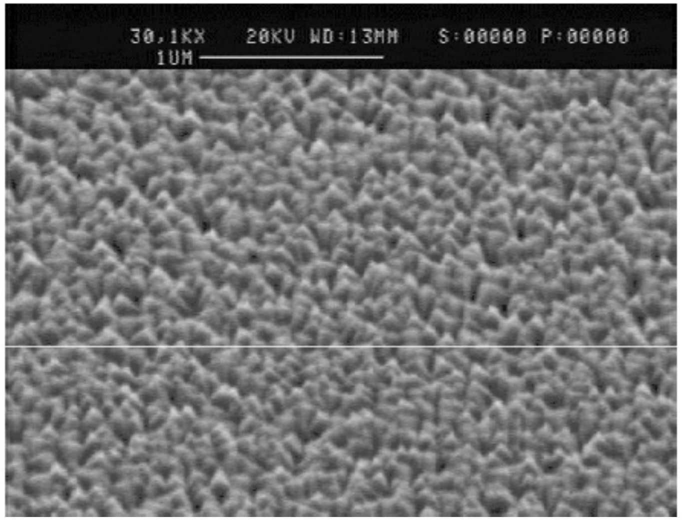
  → Requires activation



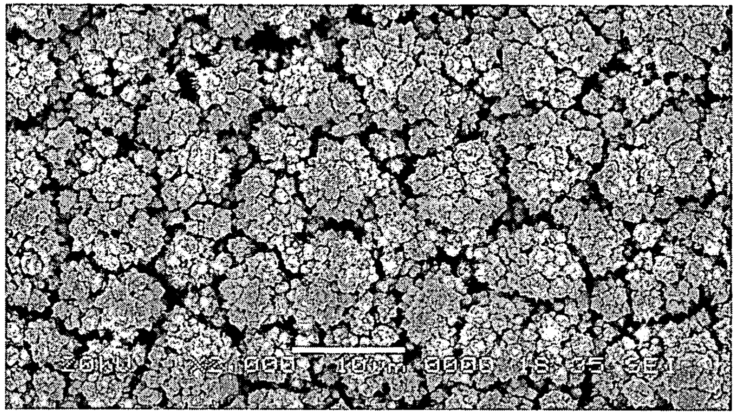
- Charge injection: 1-8mC/cm^2

Porous - Rough structures

TiN



Platinum grey

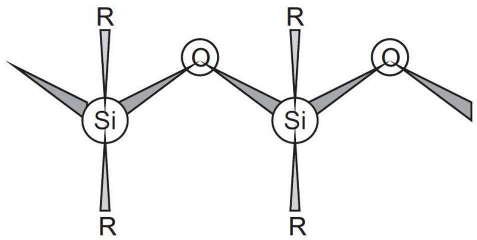


Electrode material	Q_{inj} (mC/cm^2)	Water window
Platinum	0.1-0.2	-0.6 to 0.8V
Titanium nitride	1	-0.9 to 0.9V
Platinum black	1	-0.6 to 0.8V

Insulating materials

- Many insulating materials but few are suitable for direct immersion into biological systems
  - Evaluation under saline conditions is required
  - In vitro vs in vivo
- Accelerated testing
  - insulator monitor, 4-point resistance,
  - Young's modulus monitor, surface bonding monitors
- Accelerating degradation
  - Elevated temperature (but can alter chemical reactions)

Silicones encapsulation / packaging



- Long-lasting material
- **Polymer** with simultaneous presence of organic groups attached to inorganic atoms

- Silicone elastomers (rubbers)
  - Molding, injection, spin-coating, printing
  - Cross-linked polymer

- Soft polymer : elastic modulus range: 10 kPa – 10 MPa

- Very good protection over corrosion of silicon and oxidizable materials
- Very good electrical insulators (esp. Fluoropolymers)

Take-home message
The « optimal » electrode

- Low energy consumption for stimulation
- Effective charge injection at geometrically small electrode sites
- High reversible charge injection limits
- Low polarization at the phase boundary
- Low and stable impedance

- Low frequency dependence of the impedance
- Low electrochemically induced noise

- Long term stability over decades in the body
- Biotolerance of the materials