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Production of conductive composite electrodes for extracellular recording and stimulation

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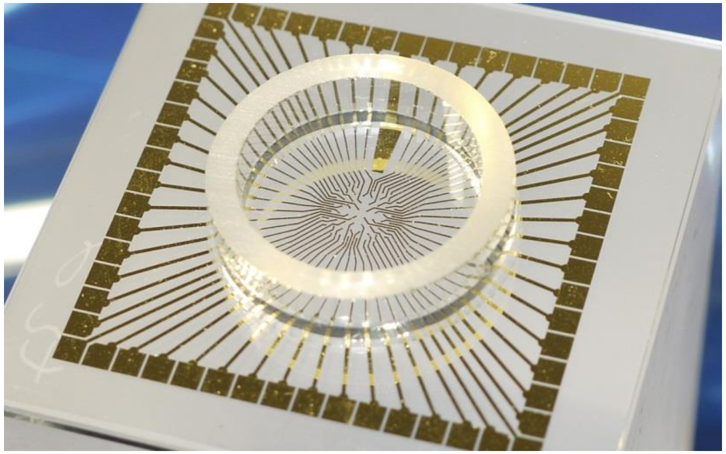
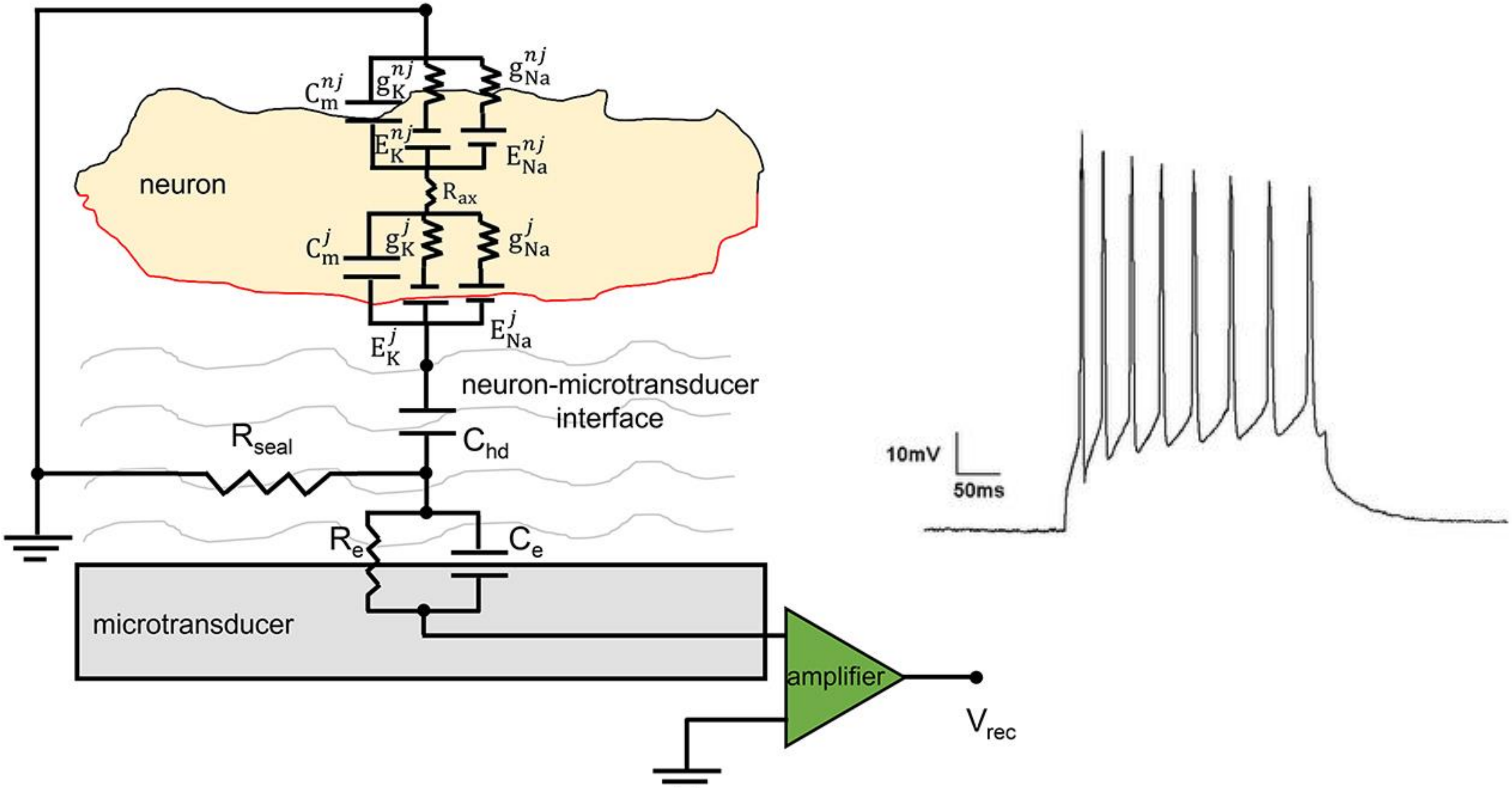
Multielectrode arrays (MEAs)

- MEAs are arrangements of electrodes allowing the targeting of several sites in parallel for extracellular recording and stimulation
- Used by bioscientists to understand fundamental biological processes (e.g. ageing)
- Commonly used in the fields of neurobiology and cardiac electrophysiology



Source: Multi Channel Systems

Cellular stimulation and recording



Massobrio, Paolo, Giuseppe Massobrio, and Sergio Martinoia. *Frontiers in neuroscience* 10 (2016): 282.

Typical neurobiological applications

- *In vivo* – implantable devices for deep brain stimulators (Parkinson’s disease)
- *In vitro* - single-cell cultures or acute brain slices

- Drug testing; safety pharmacology studies
- Neuroregeneration
- Developmental biology
- Microencephalograms (EEG)
- Microelectroretinograms (ERG)

Key features

- Allow placement of multiple electrodes (better spatial resolution compared to patch clamp techniques)
- Able to set up controls within same experimental setup
- Can record simultaneously from multiple sites, or select different recording and stimulations sites
- Non-invasive

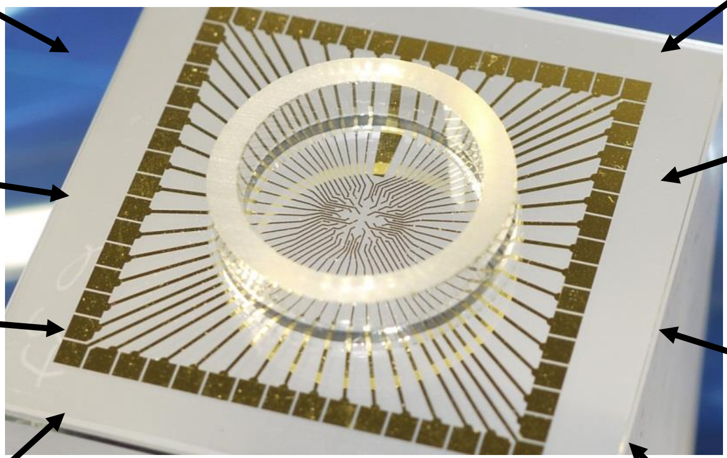
Current technology

Biocompatible (typically Au, TiN, ITO on glass)

Well-defined geometries

Reasonable electrode density

Excellent chemical and thermal stability (can be autoclaved/ sterilised)



Expensive (>£100s)

Limited designs available – no spikes

Electrodes tracks often exposed

Difficult to produce at scale

Economic implications

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- Existing technologies are very expensive:
  - MEAs with 8 or more electrodes cost ≥ £100
    - Can reuse a few times depending on coatings
  - Centre for Process Innovation's National Industrial Biotechnology Facility to monitor and optimise fermentation processes use disposable cuvettes incorporating 2 electrodes costing ca. £100 each in machines holding up to 100
- Fabrication is very expensive:
  - Clean room, sputtering machine, mask aligners, spinners, lift-off and photoresists, masks, metals, etc. ≥ £1M
  - Compared to multi-material printer, e.g. J750 Stratasys ~£250k

Early trials

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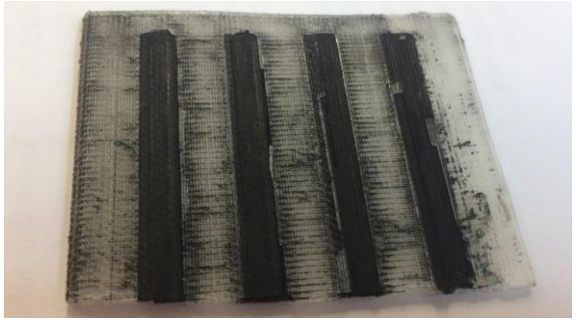
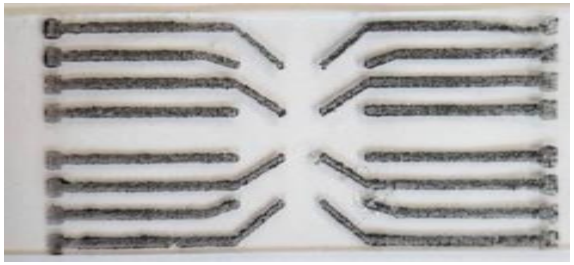
- Fused filament fabrication (FFF) of conductive filaments
  - PLA/carbon black filament from Proto-pasta
  - PLA/graphene from Haydale
  - Deposited using Ultimaker 2 and multi-material Z-Morph
    - Insufficient resolution
- Block printing and screen printing
  - Curable polyimide polymer thick film silver conductor (ESL Electroscience)
  - Allowed for use of glass substrates
  - High productivity
    - High curing temperature >320°C
    - Issues with repeatability and robustness

Issues

- Conductive PLA printed inside a clear PLA substrate on Z-Morph had indistinct layers



- Irregular surface result from block printing using conductive silver paste on glass



- Smearing of ink during manual screen printing of fine detail

Additive manufacturing strategy

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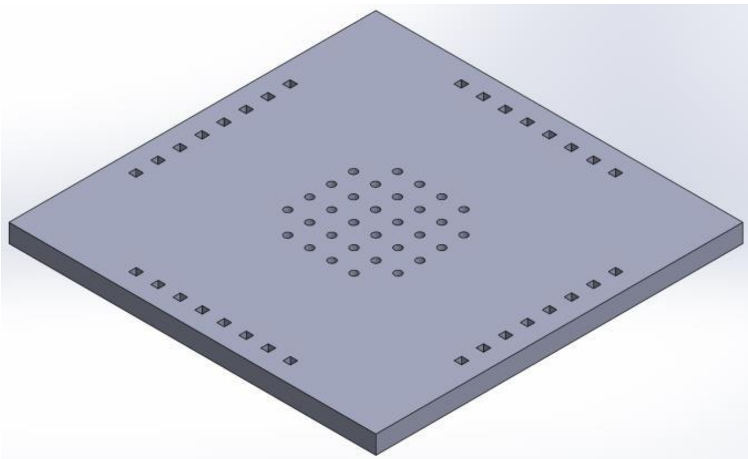
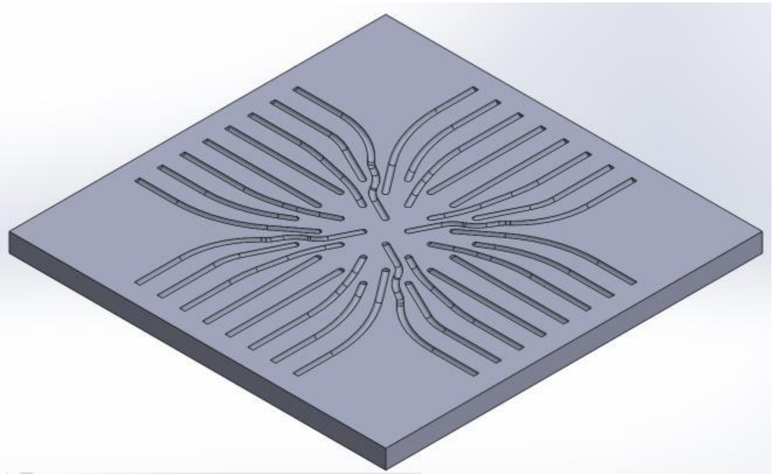
- Multi-material printing based on FFF due to lack of commercially available conductive inks for direct writing of electrodes
  - Insufficient resolution and interconnects observed
- Strategy: to combine direct write and additive manufacturing by printing channels that can be filled with conductive materials
- Issue: conductive materials difficult to extrude through channels.
- Solution: Modify viscosity and use open channels

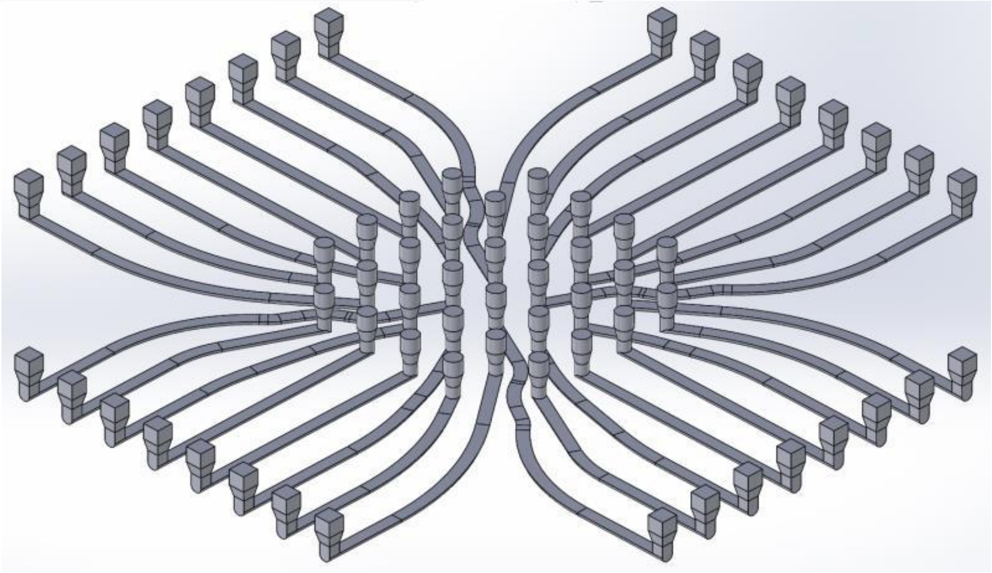
Electrode impedance

- Low impedance is necessary to achieve good signal-to-noise ratio (>5:1 preferred)
- Impedance of 30 µm TiN microelectrodes is < 100kΩ (250-400 kΩ for smaller electrodes)
- Charge transfer depends on surface area and thickness of the electrode-electrolyte double layer
  - Often limited by electron and ion transfer rates in the coating
- Impedance between electrodes dependent on height and spacing of electrodes

MEA layout







Note: 0.7 mm channels
Closest approach 0.14 mm

Tested electrode materials

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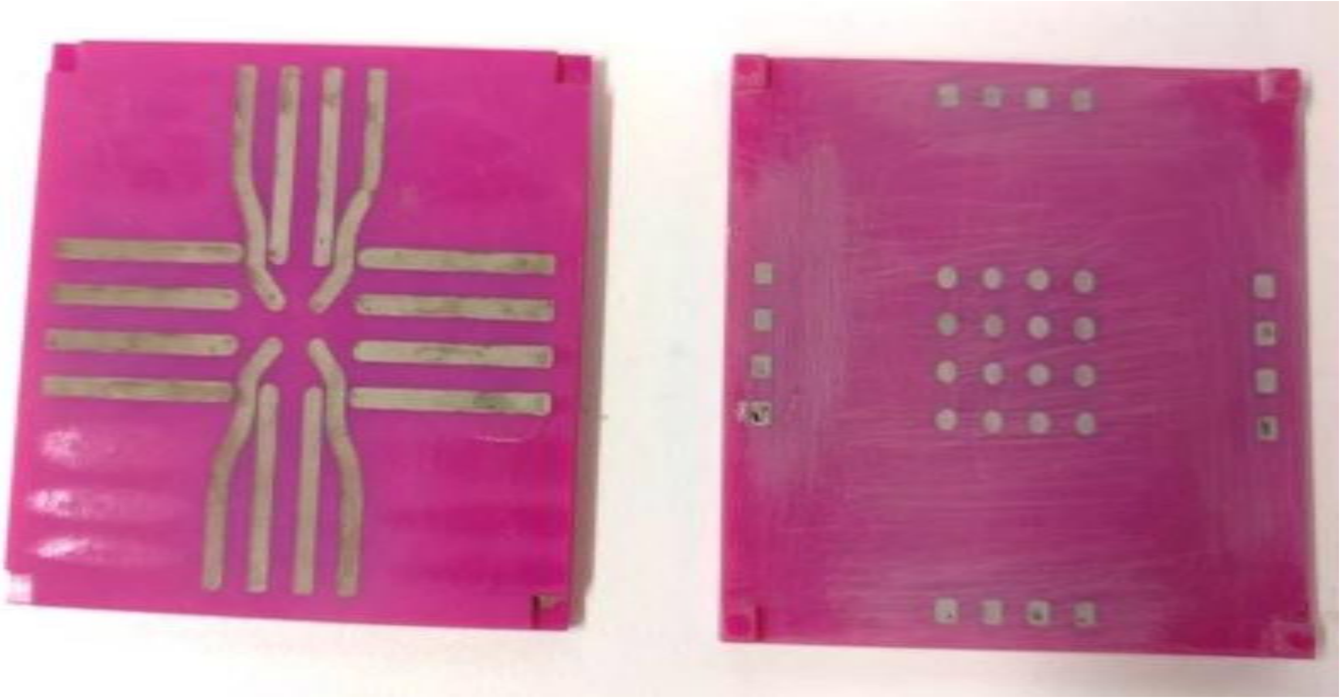
- Conductive carbon nanotubes (CNT) and polydimethylsiloxane (PDMS)
  - Two part PDMS (Sylgard 184, Dow Corning) with 20% CNT (by mass), degassed and cured at 80°C for one hour.
    - Resistance: 152 kΩ ± 111 kΩ
- Conductive silver paste (Sigma Aldrich)
  - Silver paste dispersed in α-terpineol
  - Viscosity high so diluted with additional α-terpineol at ratio of 3.35:1 (paste:α-terpineol) by mass to aid injection

Conductive silver paste

- Particle size: 200nm (80%), <5μm (20%)
- Solid content: > 75%
- Viscosity: 100,000-300,000 (cps) @ 0.4rpm
- Curing Condition: 120-150 °C for 30-60 min
- Flash point: 88 °C
- Dispersion matrix: α-Terpineol
  - Major constituent of aroma of lapsang souchong tea due to pine smoke drying process!

Filled tracks



Diluted paste was injected directly into channels and excess removed. Fill was reduced by evaporation of solvent. Repeated fills after evaporation was required.

Interface

- Silver paint was used as an alternative to chemical or vapour-deposited platinum black on the surface, as well as the joining medium between the two parts.
- The structure after evaporation of the dispersing agent was a deposit of micro- and nano-particles, with 80% of particles being 200nm in diameter and the remaining 20% <5 µm in diameter.
- Dispersed in 2-methoxy-1-methylethyl acetate, n-butyl acetate
- Excellent surface conductivity – used as replacement for solder
- Alcohol resistant, esp. ethanol, for cleaning

Final process

1. Print top-half and bottom-half CAD model on Stratasys J750 – 105 minutes for 10 MEAs
2. Remove any support material with high pressure water cleaner – 30 minutes
3. Mix 25g containers of silver paste with 9.3ml of acetone per container and pour into syringes – 30 minutes
4. Inject paste into channels 5 times (average number of injections) – 30 minutes per injecting session, 120-minute wait between sessions
5. Evaporate any remaining dispersing agent in over at 80°C for 60 minutes

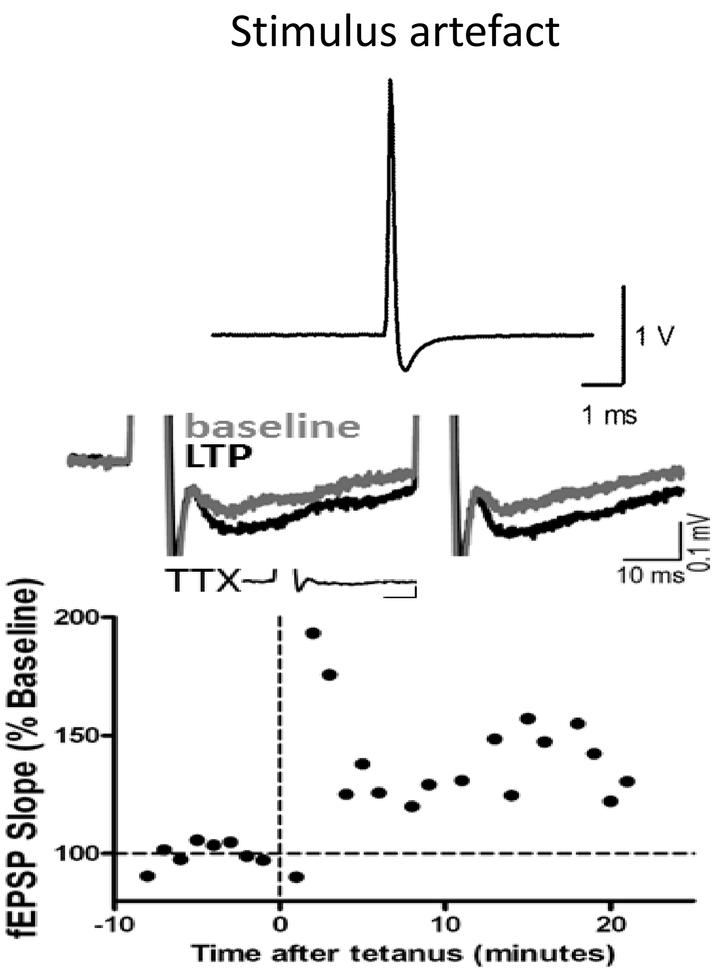
Final process

6. Surface finish top and bottom parts to remove any dried paste spilled – 30 minutes
7. Apply silver paint to end of each channel on bottom part and each corresponding connector/electrode on top part, and a small drop of superglue to each corner of bottom half – 20 minutes
8. Clamp and leave to dry for 360 minutes
9. Apply silver paint to top surface for 10 minutes
10. Cure MEA at 120°C for 10 minutes

This results in an average time of about 24 hours to manufacture a batch of 10 MEAs at a cost of £35.57 per MEA

Trials

- MEAs used to stimulate nervous tissue ex vivo in the laboratory of Frances Edwards with Damian Cummings at UCL.
- fEPSPs were recorded by electrode placed in CA1 stratum radiatum in response to a 20 ms, 20V square stimulation pulse applied to CA3 stratum pyramidale/oriens
- The plot shows that these responses stay stable over time (within biological variation).



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