FLAG-ERA JTC 2015

Graphtivity

Graphene-based optoelectrochemical sensor for the simultaneous monitoring of the electrical and chemical activity of single cells

Starting point: FLAG-ERA JTC 2015

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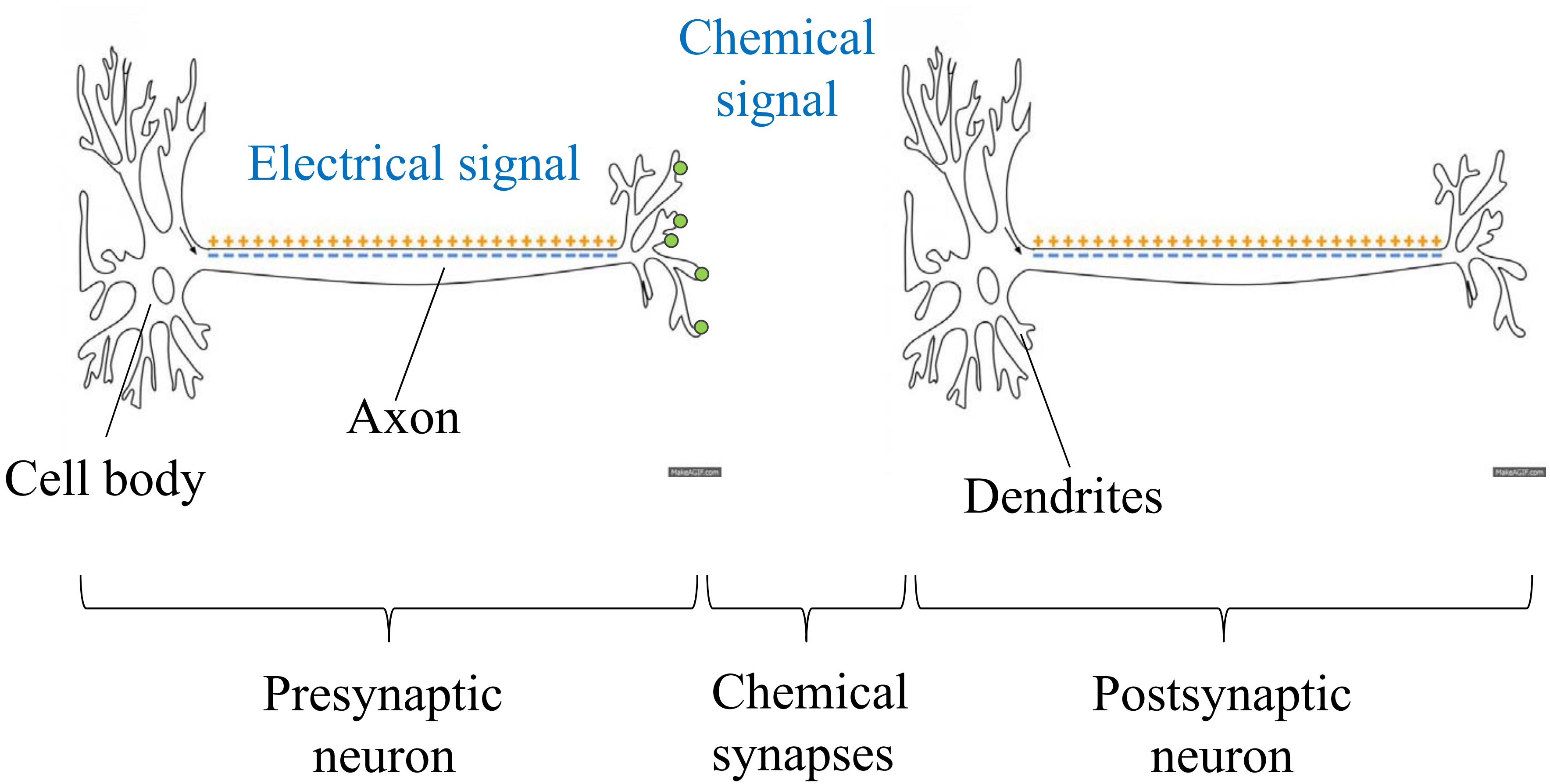
…should be able to report biological cell generated changes in the membrane surface potential, but also on chemical signals (neurotransmitters, ions, etc.) involved in cell communication; detection of electric field and chemical gradients at membrane/cell surface. Time lapse images of surface potential changes or release of neurotransmitters.

How neurons communicate?



Obs.: Animation from https://en.wikipedia.org/wiki/Action_potential

Neurotransmission in numbers

- Dimensions of the selected cells: cell body of ~10-30 µm and neurites of ~20-60 µm
- Dimensions of a synaptic cleft: width of ~20 nm, diameter of ~0.4-1 µm
- Dimensions of secretory vesicles: ~ 25-75 nm
- Concentrations of neurotransmitters:
  - in vesicle: 60-210 mM (glutamate); 110 mM (dopamine)
  - in cleft: ~1-3 mM (glutamate; but decreasing with τ = 1-2 ms)
  - outside cleft: ~ 10 µM (glutamate; microns away from the cleft)
- Amplitude of the action potential (AP): When assessed with microelectrode arrays, from tens to hundreds (rarely thousands) of microvolts (very much function of the cellular model and experimental conditions)
- Propagation speed of the AP: from 0.18 m/s to 150 m/s (slower in cells other than neurons)

Partner Number	Country	Institution/ Department	Name of the Principal Investigator (PI)
1 Coordinator	Germany	Ruhr-Universität Bochum / Analytische Chemie - Elektroanalytik & Sensorik	Wolfgang Schuhmann
2	Belgium	Université catholique de Louvain / Institute of Information and Communication Technologies, Electronics and Applied Mathematics	Sorin Melinte
3	France	National Center for Scientific Research / Institute of Electronics, Microelectronics and Nanotechnology	Rabah Boukherroub
4	Italy	The Italian Institute of Technology / Depart-ment of Neuroscience and Brain Technologies	Axel Blau
5	The Netherlands	Brains On-Line B.V.	Ben Westerink, Thomas Cremers
6	Romania	International Centre of Biodynamics	Szilveszter Gáspár

Main idea of Graphtivity (1)

Electrochemical current, be it non-Faradaic or Faradaic, impacts the Surface Plasmon Resonance (SPR) response / image of conductive thin films

↓

SPR imaging of conductive thin films can provide high resolution images of electrochemical current density distributions

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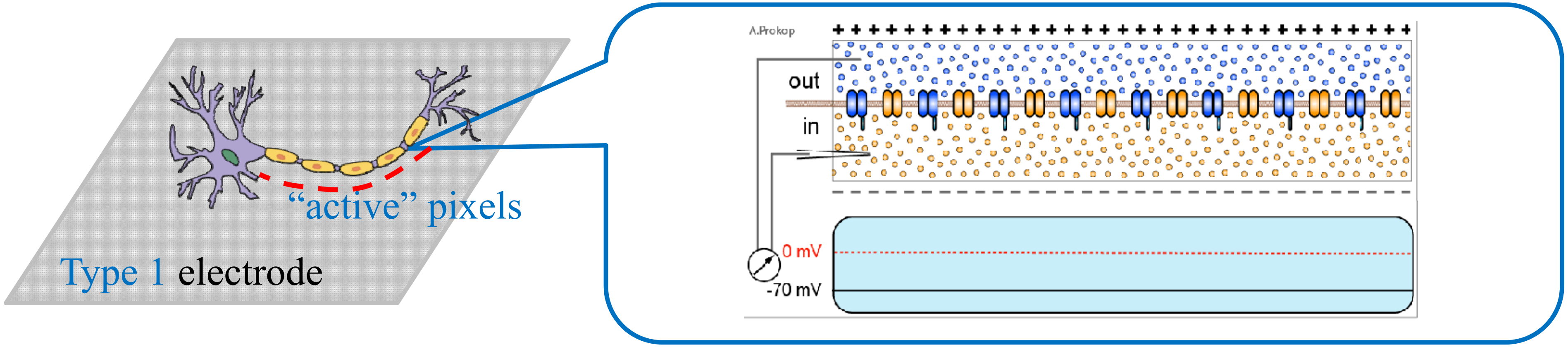
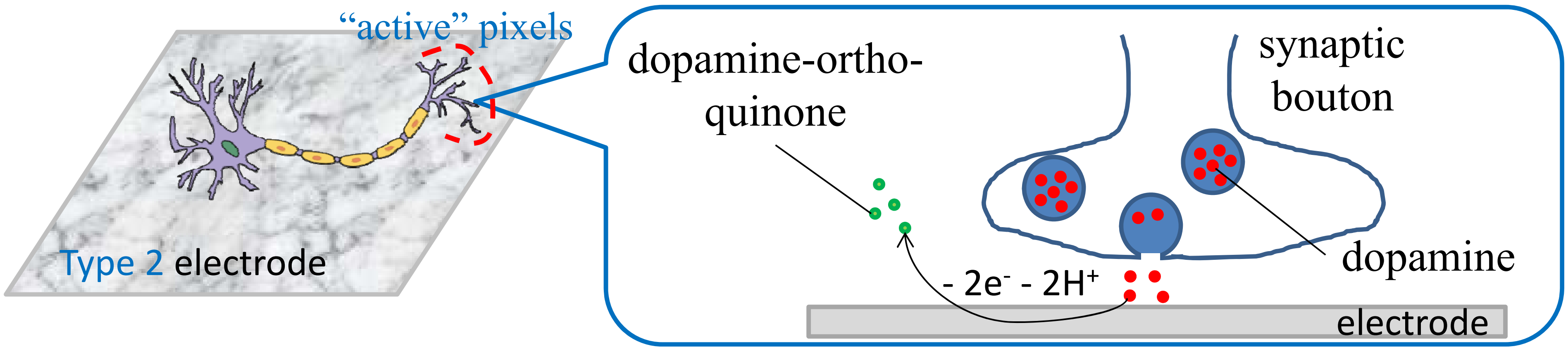
SPR images recorded at high frame rates are suitable to observe both the propagation of action potentials and the release of neurotransmitters

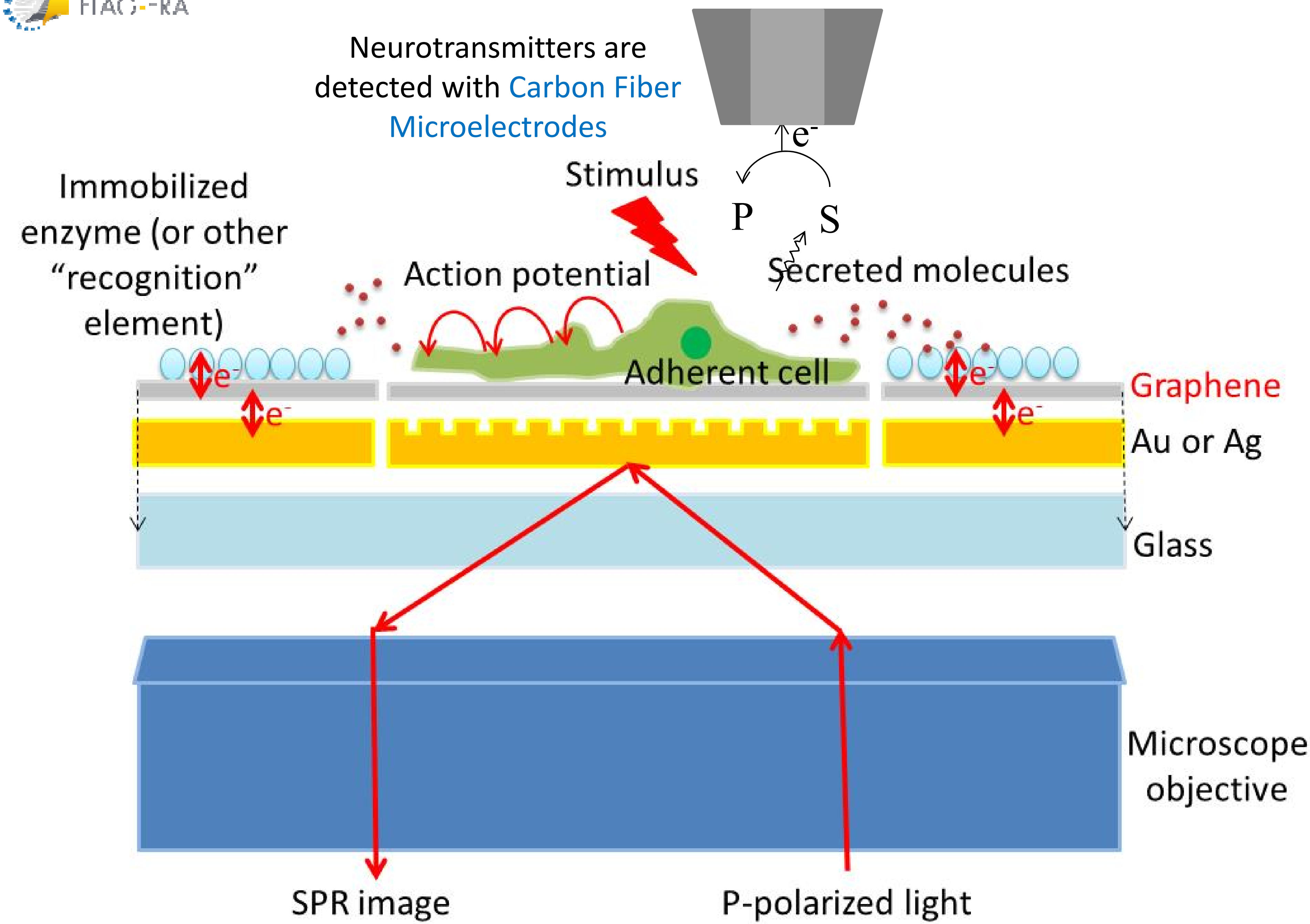
Main idea of Graphtivity (2):



Action potentials = Na^+ and K^+ ions moving through ion channels in a highly orchestrated manner = non-Faradaic current which travels along the axon => it will impact the SPR image

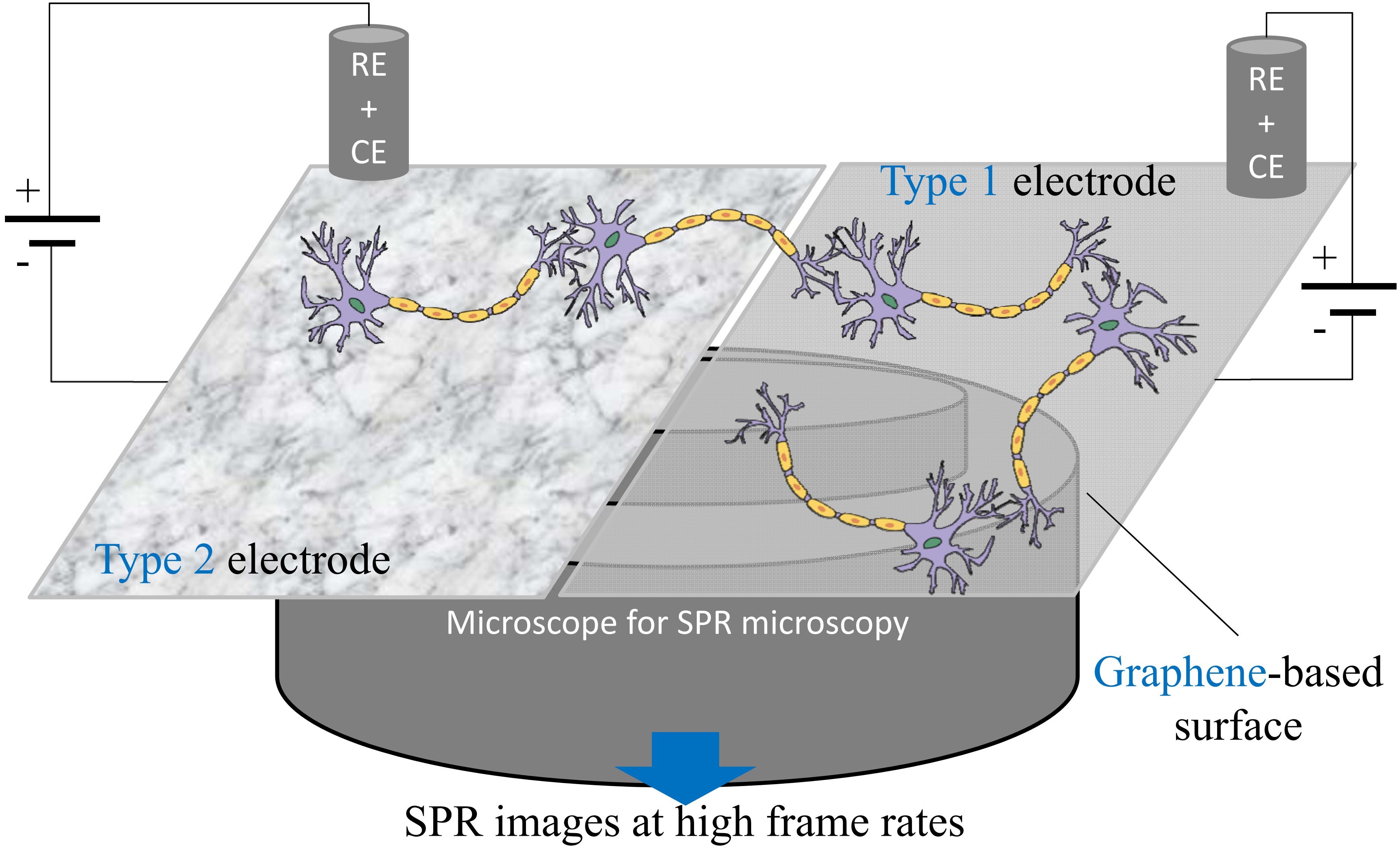


Neurotransmitter release can be translated into a small localized Faradaic current through electrooxidation => it will show up in the SPR image



Neurotransmitters are detected with Carbon Fiber Microelectrodes
e-
Stimulus
P
S
Immobilized enzyme (or other "recognition" element)
Action potential
Secreted molecules
e-
e-
Adherent cell
e-
e-
Graphene
Au or Ag
Glass
Microscope objective
SPR image
P-polarized light

How is neurotransmission observed in Graphtivity:



Challenges:

- Modify electrodes of the same planar array in order to allow either cell attachment or immobilization of biomolecules
- Develop sensitive and fast sensing chemistries which are suitable for both electrochemical and SPR detection
- Fine-tune SPR imaging microscopy to the necessary sensitivity and speed for observing action potentials and neurotransmitter release
- Make everything robust enough to survive several days in cell culture conditions

Interaction potential with Graphene Flagship

GRAPHENE FLAGSHIP

Division 2
„Sensors“

…different complementary approaches are explored to demonstrate proof-of-principle graphene-based sensing schemes for environmental- and bio-sensing.