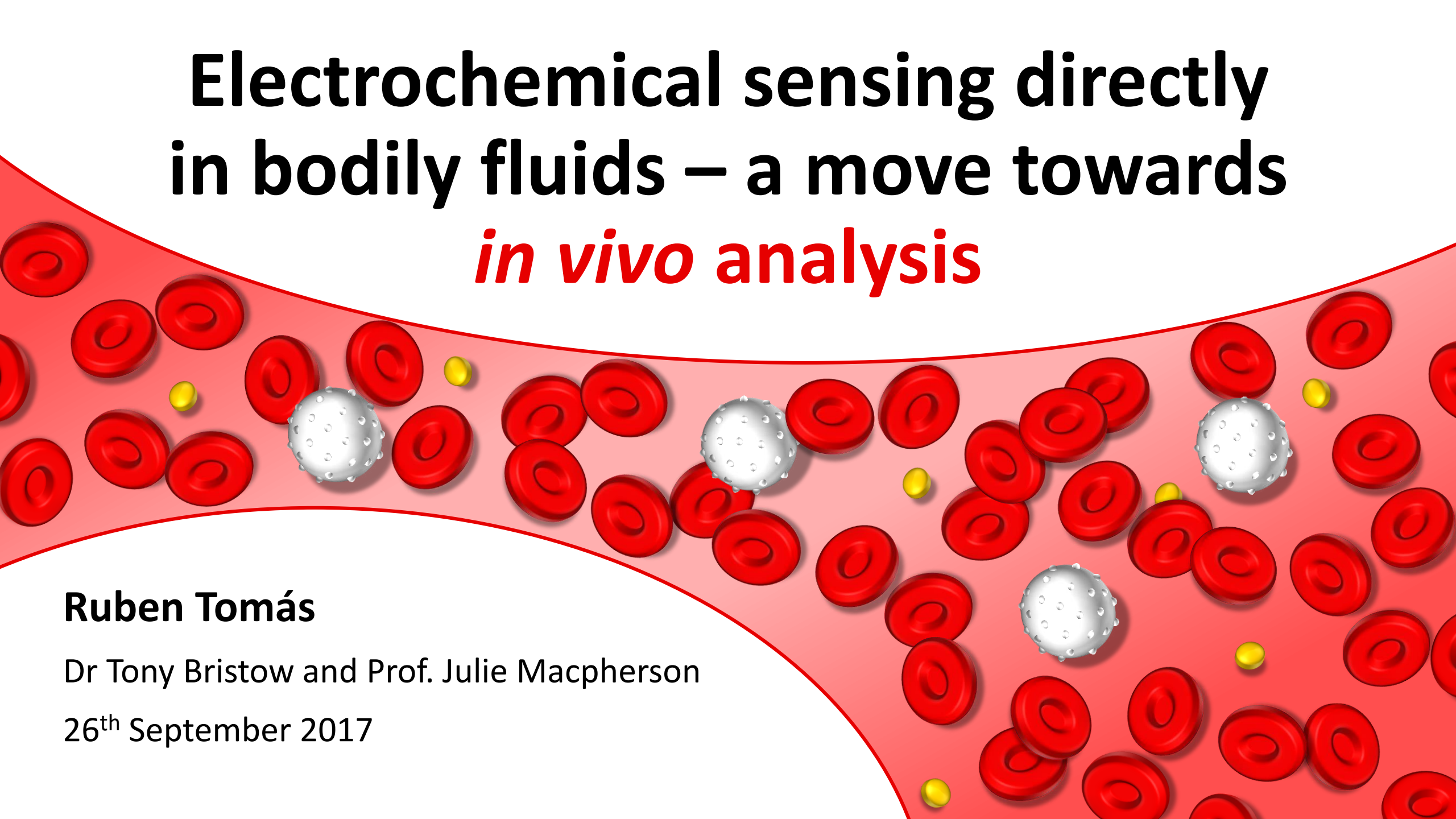
Electrochemical sensing directly in bodily fluids – a move towards *in vivo* analysis



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Outline

- Importance of *in vivo* sensors
- Mini project aims
- Why **boron-doped diamond (BDD)**?
- ***In vitro*** proof-of-concept work
- Conclusion and future work

Personalised medicine

"Providing the right treatment to the right patient, at the right dose at the right time."

– European Union

Biosensors market worth **$27.1** billion by 2022

Why *in vivo* sensors?

Monitor **health** and **disease**

Glucose biosensor

Microfluidic devices (MEDIC)

Food and Drug Administration, *Paving the Way for Personalized Medicine*, Maryland, 2013.

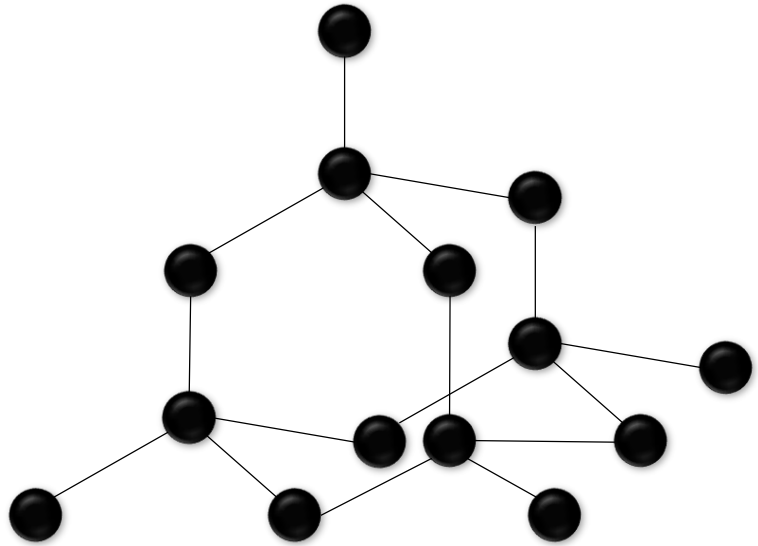
R. Salgarkar, *Biosensors Market by Application*, Hadapsar, 2017.

Aims

- To determine if **BDD** is a suitable material for ***in vivo*** electrochemical measurements of **acetaminophen (APAP; paracetamol)**

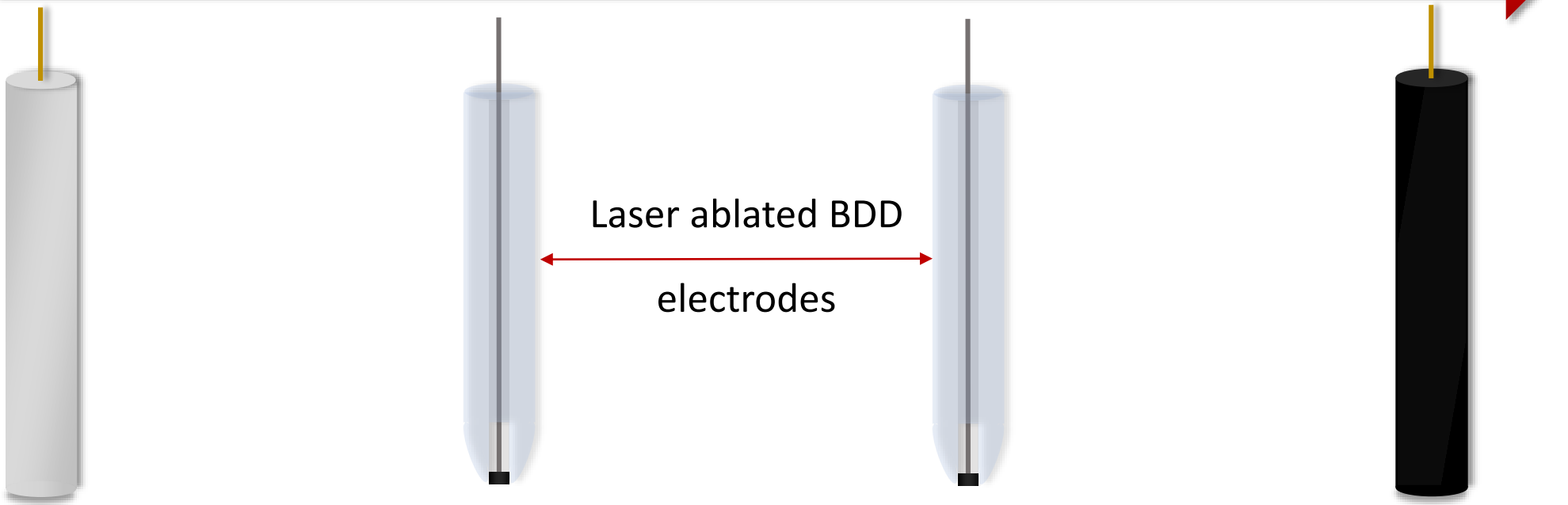
- To investigate if added **sp^2 content** is beneficial for such measurements

Boron-Doped Diamond (BDD)



- BDD has recently emerged as a prevalent material in electrochemistry

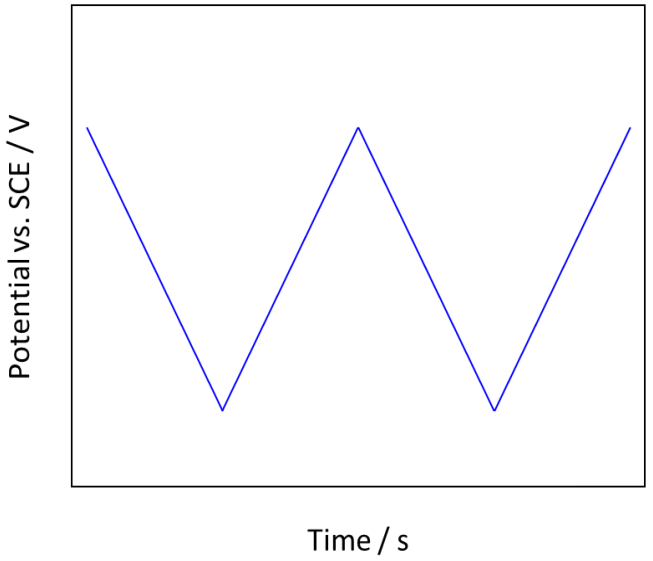
Increasing sp^2 electrode surface coverage

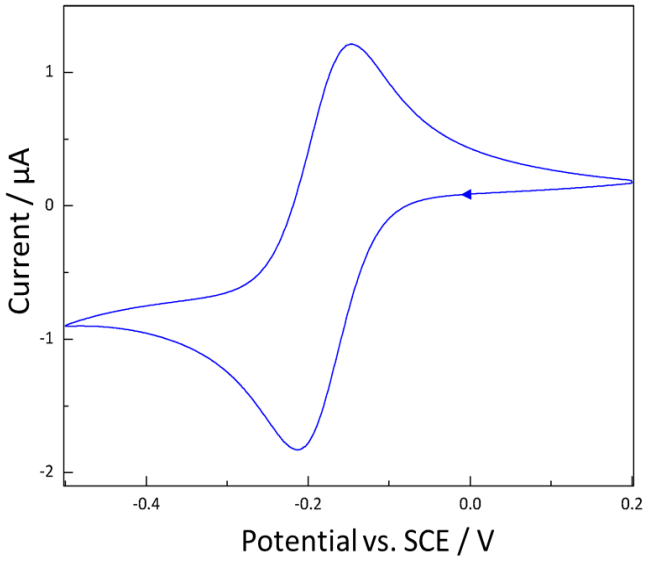


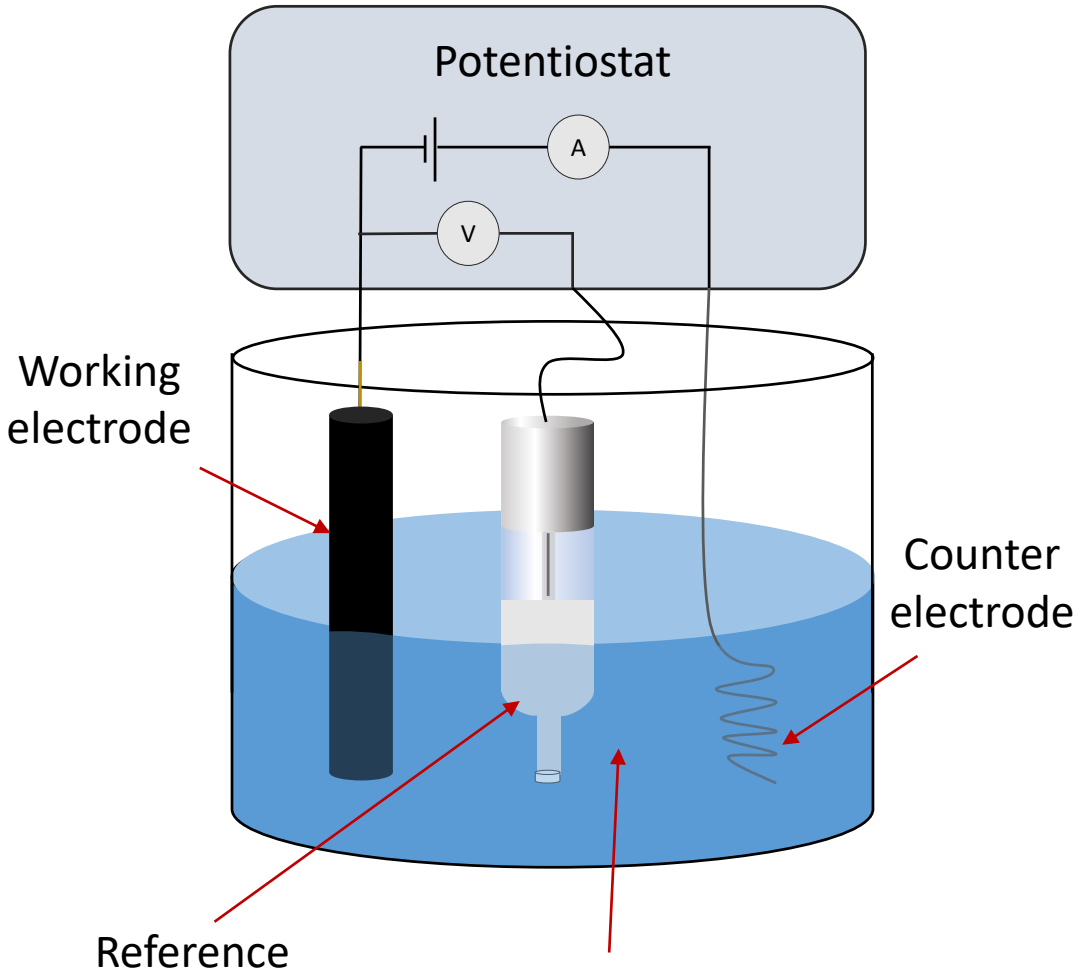
All diamond | GEN3 | GEN1 | Glassy carbon (GC)

Experimental Setup

Cyclic Voltammetry (CV)

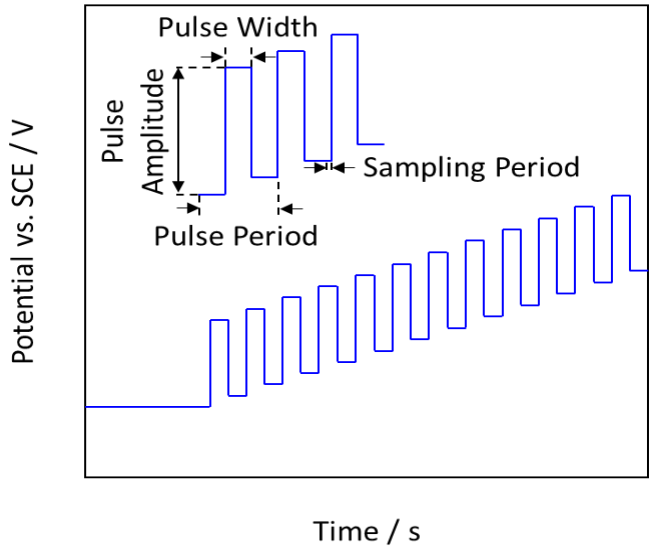


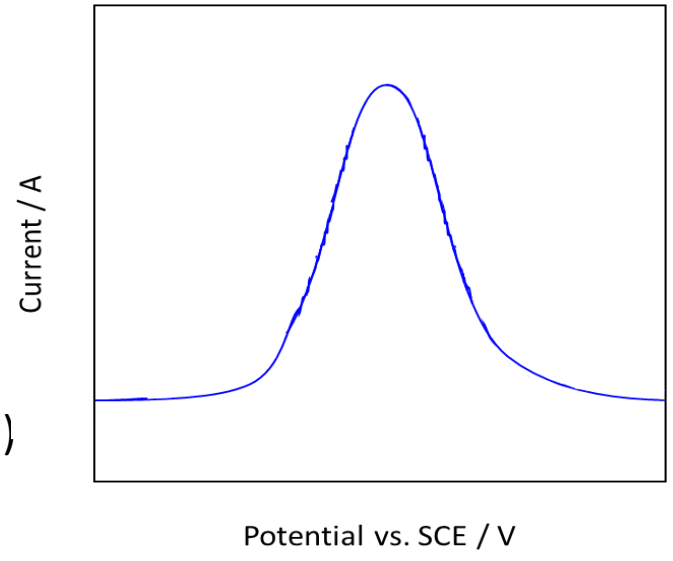




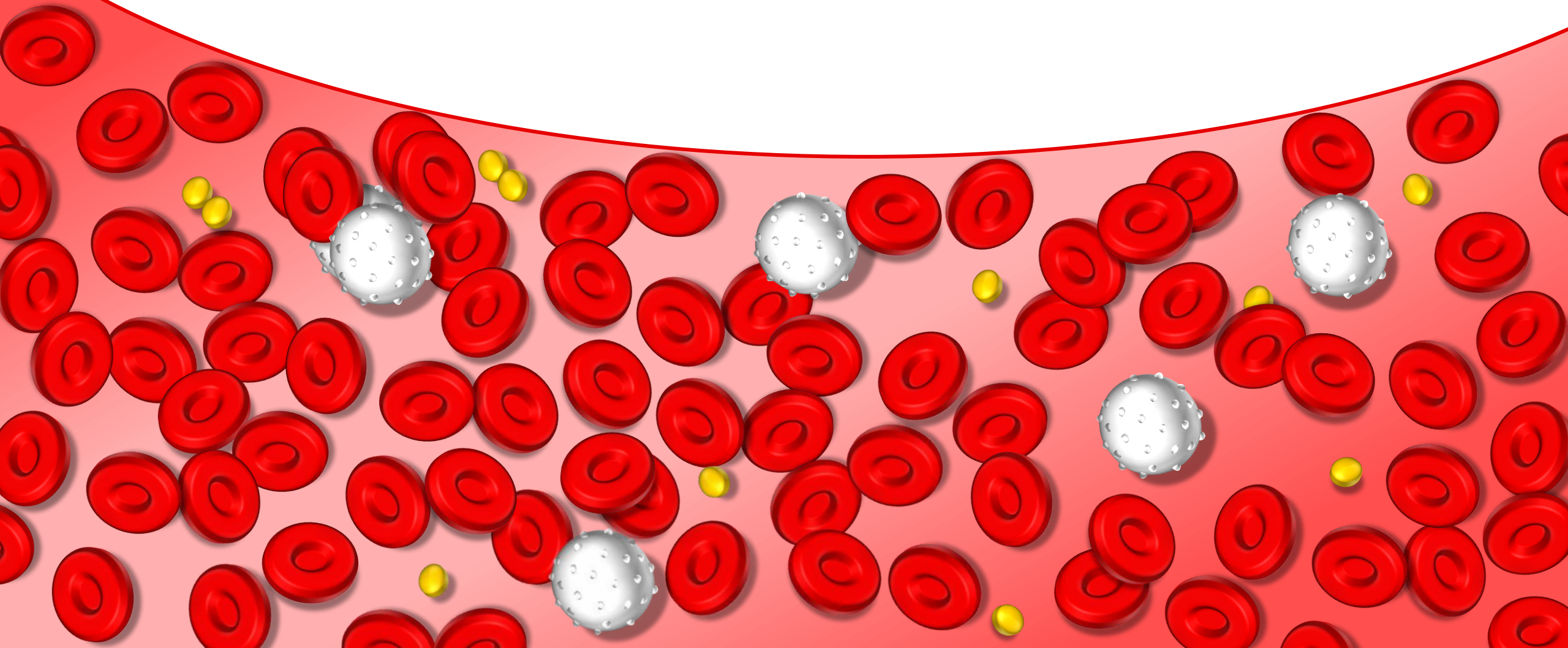
1. Simple blood model (**4% albumin**)
2. **Synthetic urine**

Differential Pulse Voltammetry (DPV)

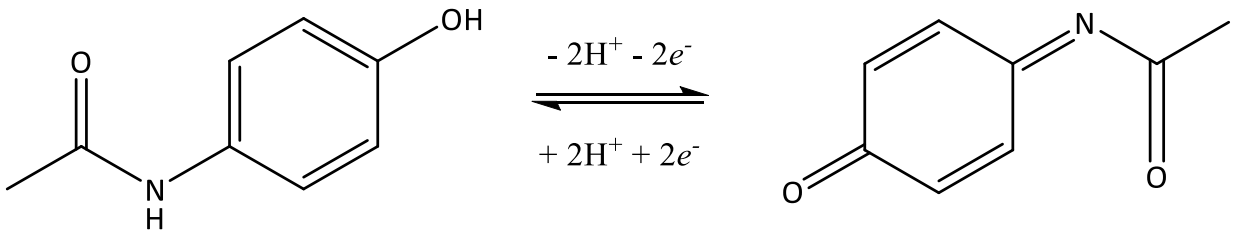


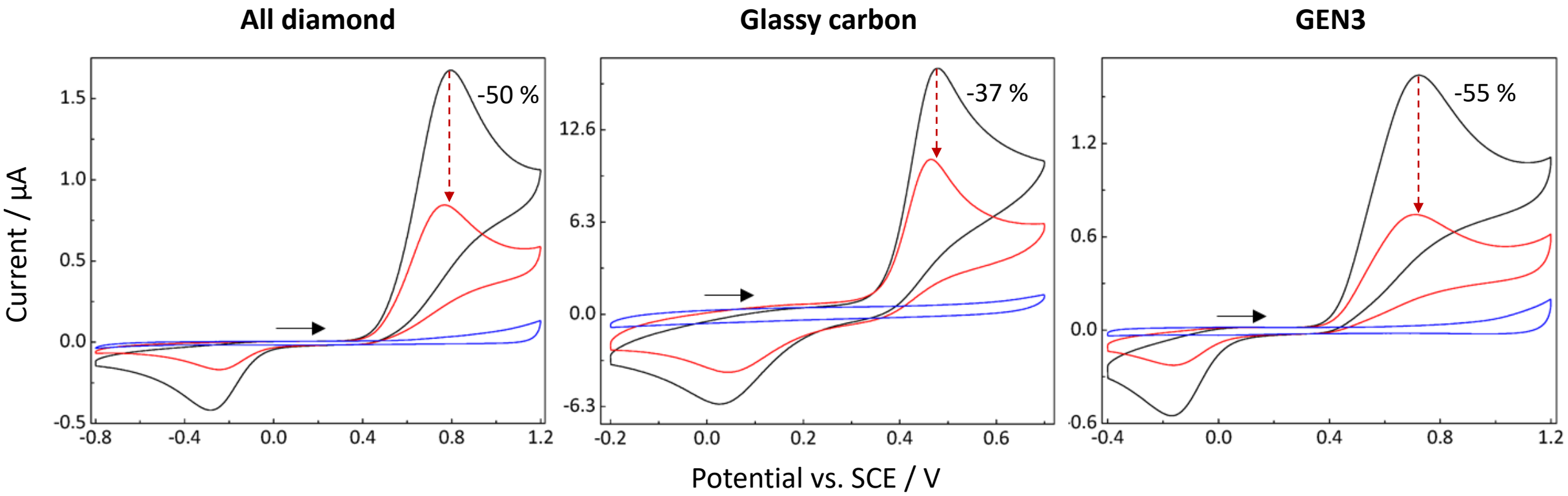


Results: 4 % Albumin



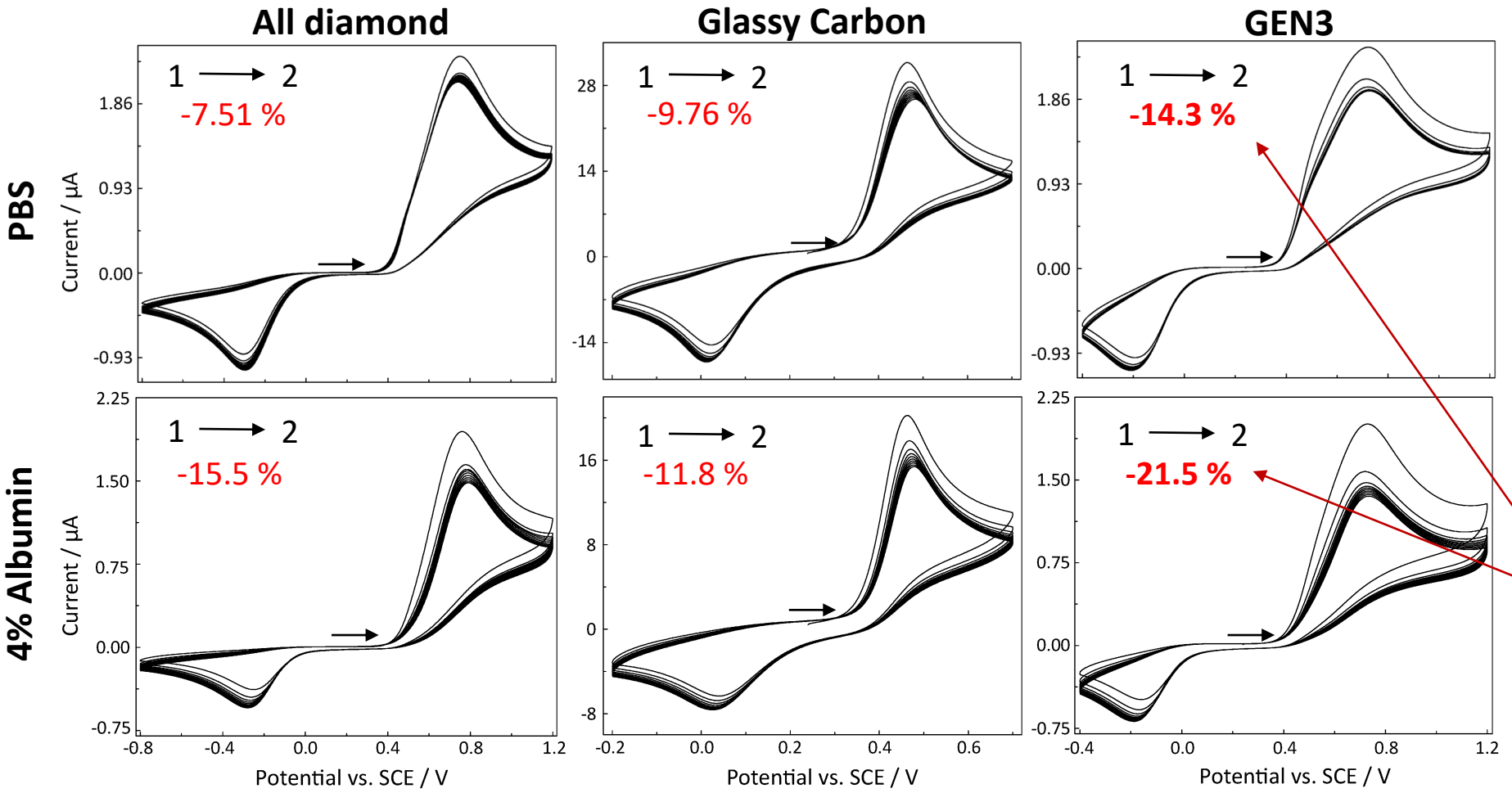
Detecting APAP in 4 % Albumin





CVs of 1 mM, 0.5 mM, and blank APAP in 4 % albumin.

Electrode Fouling in 4 % Albumin

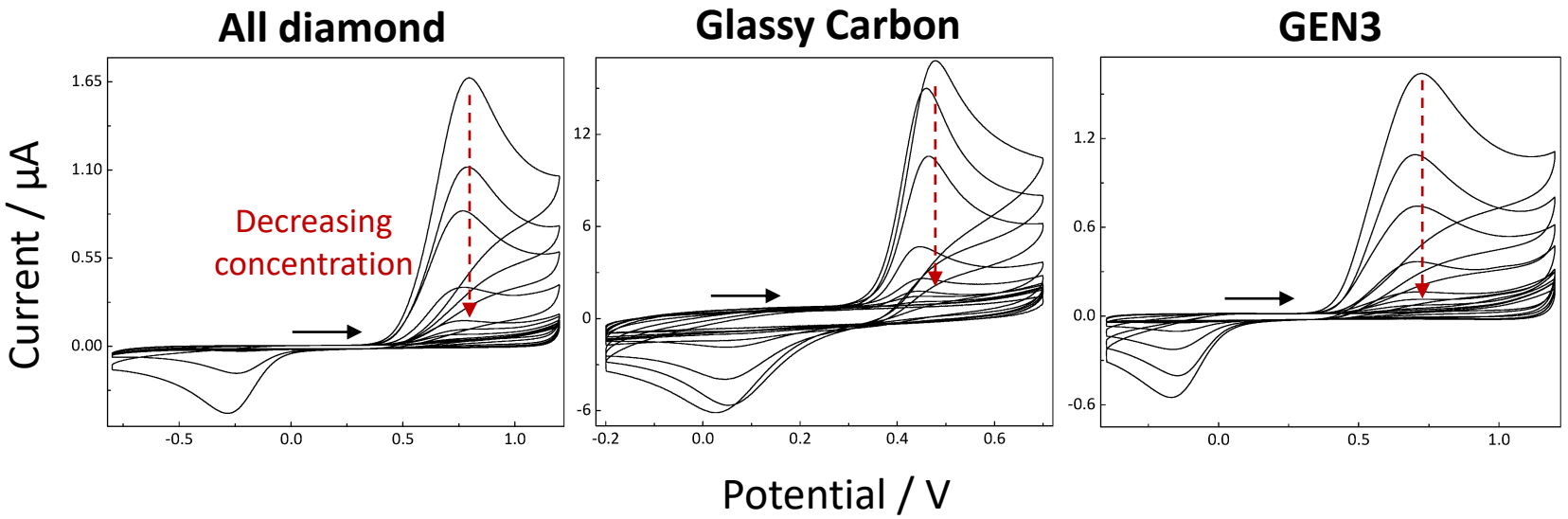


Electrode fouling is characterised by the percentage decrease in current between the first and second oxidation segments

Electrode **fabrication** significantly affected **electrode fouling**

CVs obtained of 1 mM APAP in PBS and 4% albumin (10 full scans).

Detection and Quantification Limits



CVs obtained of (0.5 µM to 1000 µM) APAP in 4 % albumin.

- **'Pits'** introduced during laser ablation **raised** the **LOD** and **LOQ**

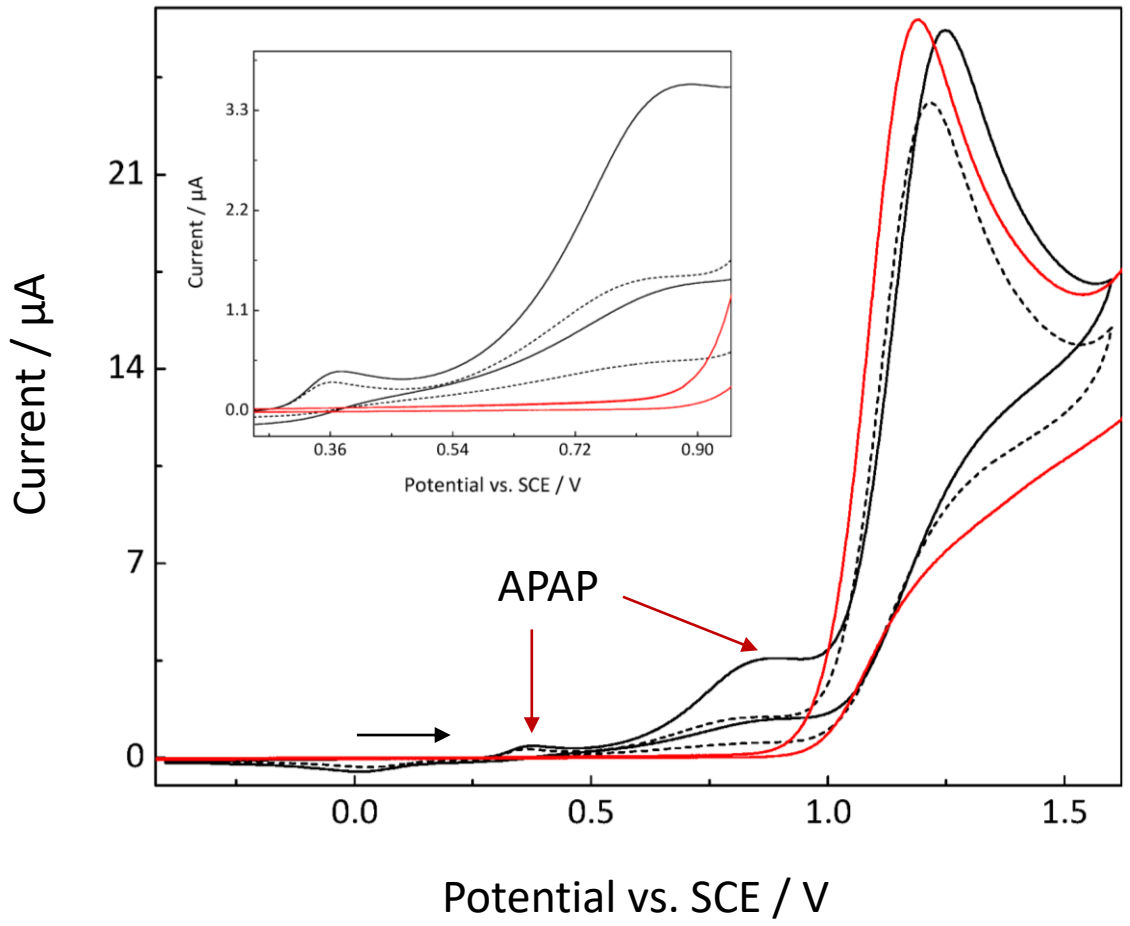
Limit of detection (LOD) and quantification (LOQ) for APAP in 4 % albumin.

- All electrodes demonstrated the necessary **LOD** and **LOQ** required for monitoring **therapeutic APAP concentrations** in **blood**

Electrode	LOD / µM	LOQ / µM
All diamond	0.428	1.30
GC	0.501	1.52
GEN3	0.652	1.97

Results: Synthetic Urine

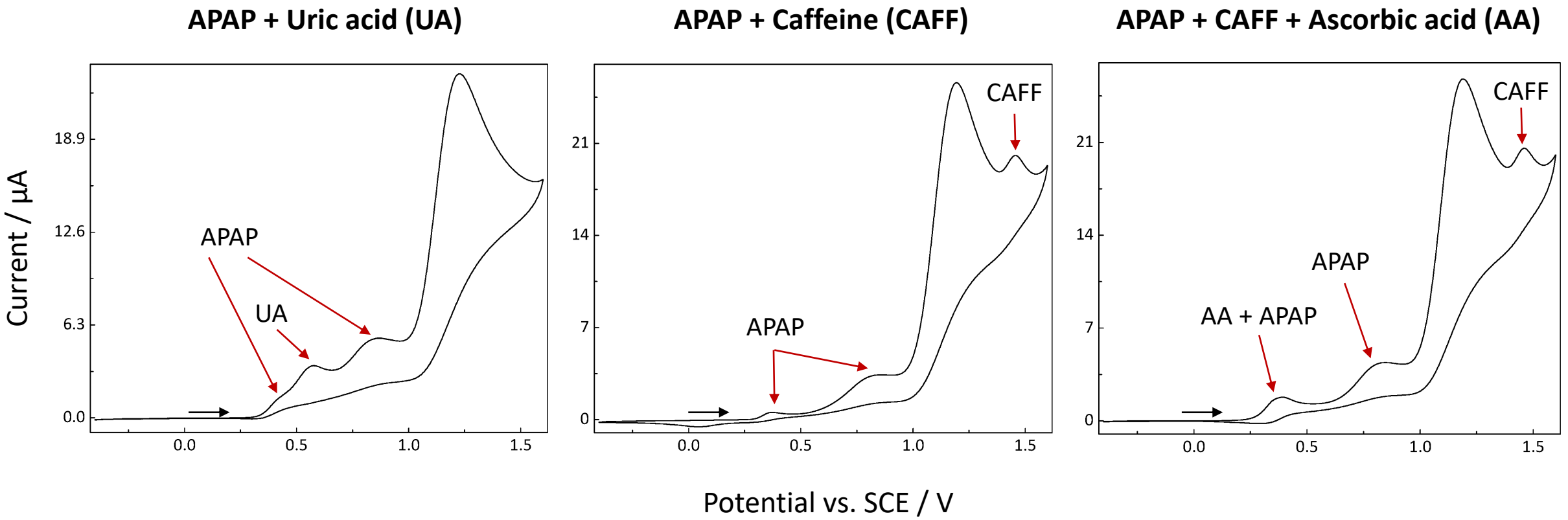
Detecting APAP in Synthetic Urine



CVs of 1 mM, 0.5 mM (dashed), and blank APAP in synthetic urine obtained using an all diamond device.

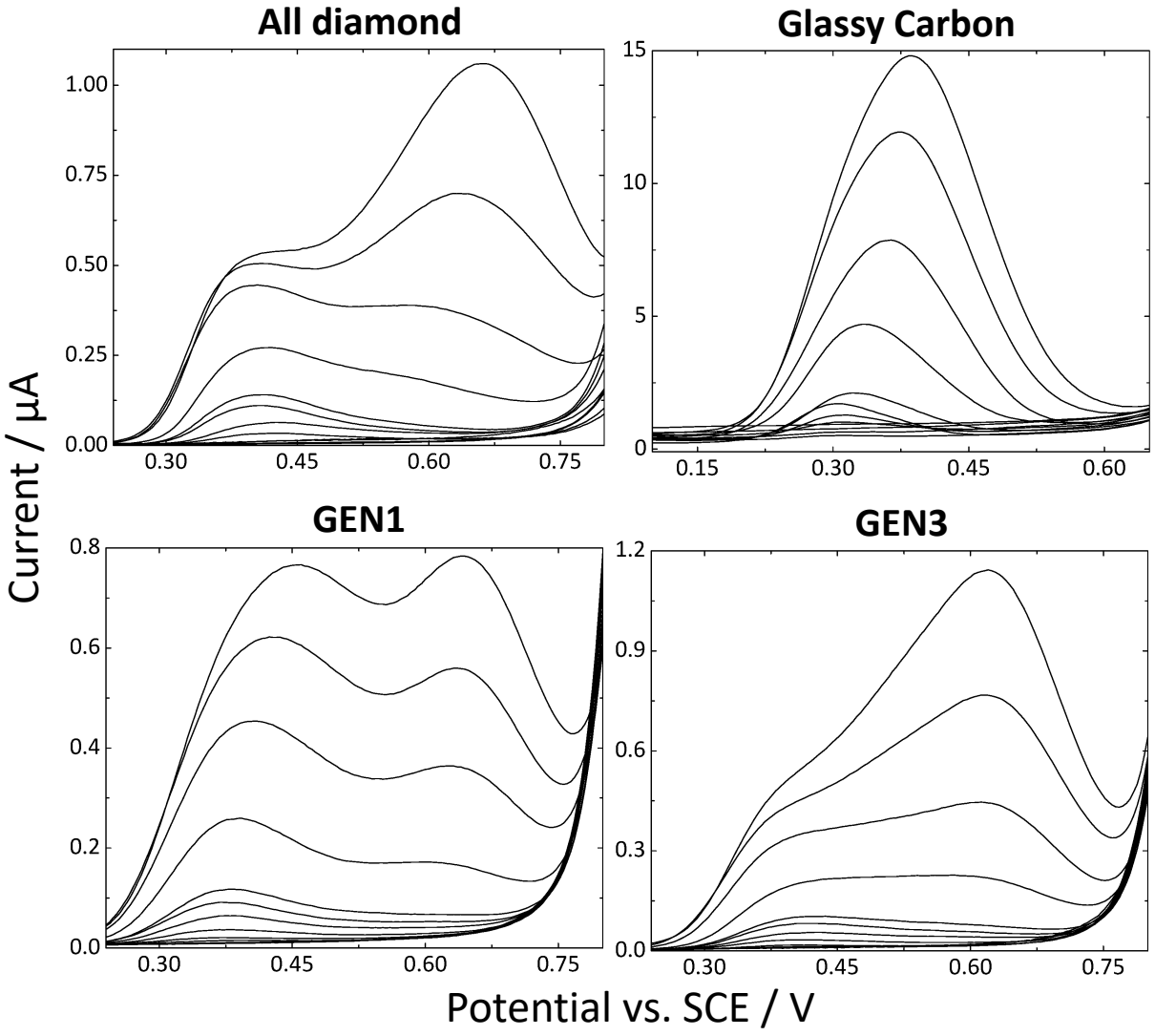
- **Two characteristic oxidation peaks** upon addition of APAP in urine could allow **better identification**
- Such capabilities demonstrate the **specificity** of BDD

Simultaneous identification in Synthetic Urine



Simultaneous detection of 1 mM APAP in the presence of additional compounds (1 mM) in synthetic urine. CVs were obtained using an all diamond device.

Detection and Quantification Limits



DPVs obtained of (0.5 µM to 1000 µM) APAP and 1 mM CAFF in synthetic urine.

LOD and LOQ for APAP in synthetic urine.

Electrode	LOD / µM	LOQ / µM
All diamond	0.0487	0.148
GC	0.266	0.806
GEN1	**0.0276**	**0.0837**
GEN3	0.286	0.867

- Electrode **fabrication** and **treatment** significantly affected electrode performance
- The all diamond and GEN1 electrodes obtained the required **LOD** and **LOQ** for measuring APAP in urine following consumption of **therapeutic doses**

Conclusions

- **Unmodified BDD** has been revealed as a prospective material for ***in vivo*** measurements of APAP in blood, obtaining the necessary **detection** and **quantification limits**, in **albumin**, required for monitoring of **therapeutic concentrations** in blood.

- **Rapid detection** of **minute** concentrations of APAP in **synthetic urine**, indicate potential use for *in vitro* measurements of human urine samples.

- Electrode **fabrication**, treatment and **sp^2 surface coverage** were found to influence electrode performance.

Future Work

- A complex *in vitro* blood model will be used.
- APAP metabolites in synthetic urine will be investigated.
- Additional pharmaceutical compounds will be studied, such as aspirin and ibuprofen.
- In the long-term, miniaturisation of BDD electrodes will be required for use as an *in vivo* sensor.

Acknowledgments

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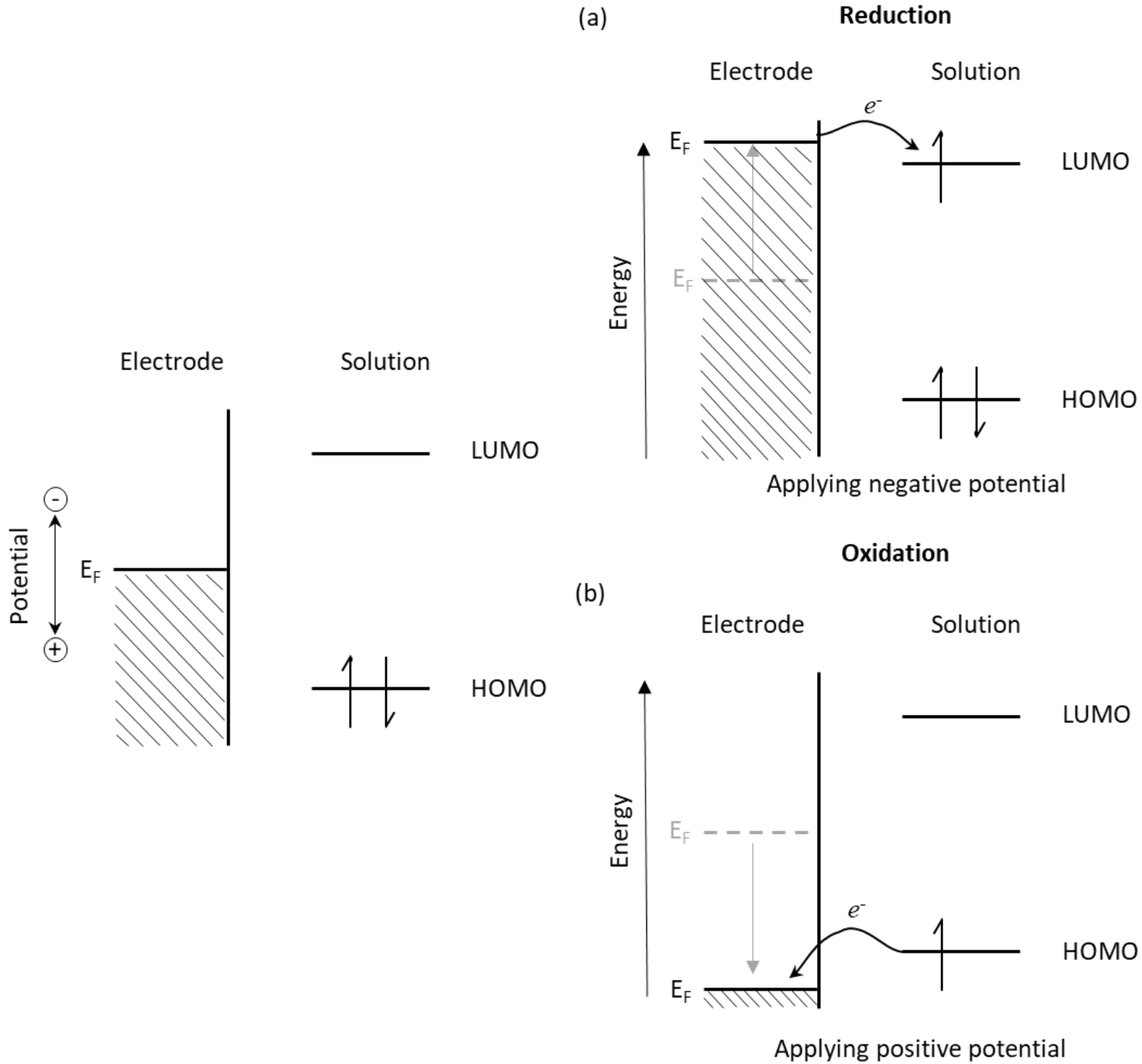
WARWICK
THE UNIVERSITY OF WARWICK

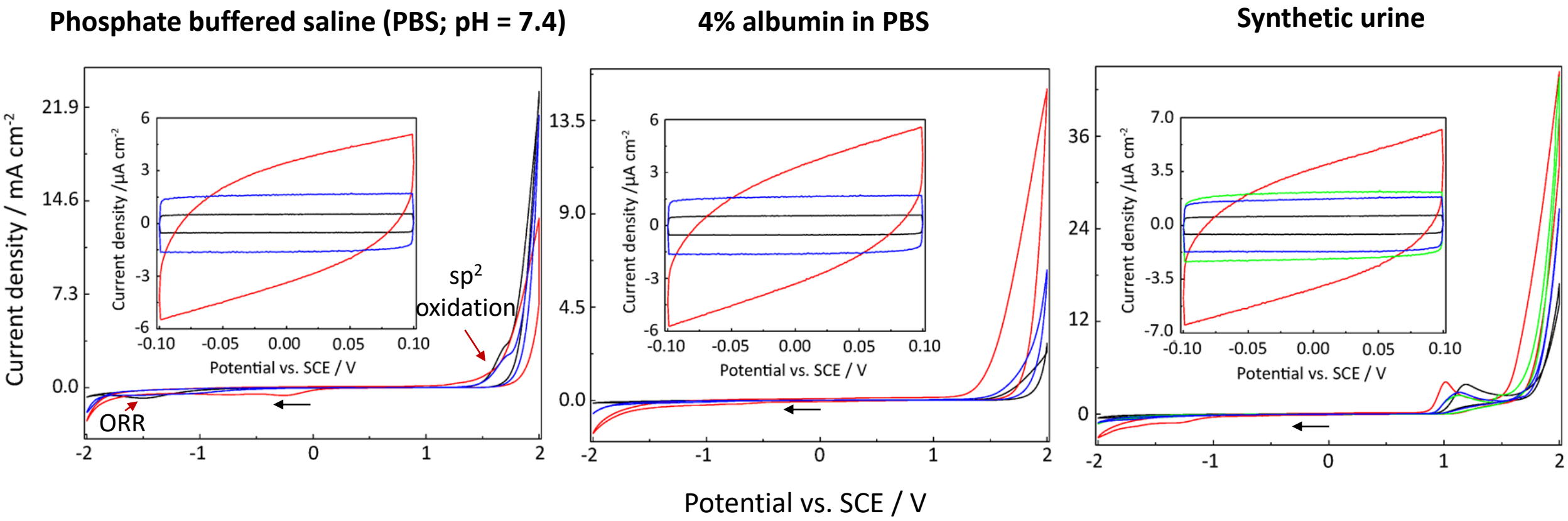
AstraZeneca

MAS CDT
Molecular Analytical Science Centre for Doctoral Training

EPSRC
Engineering and Physical Sciences Research Council

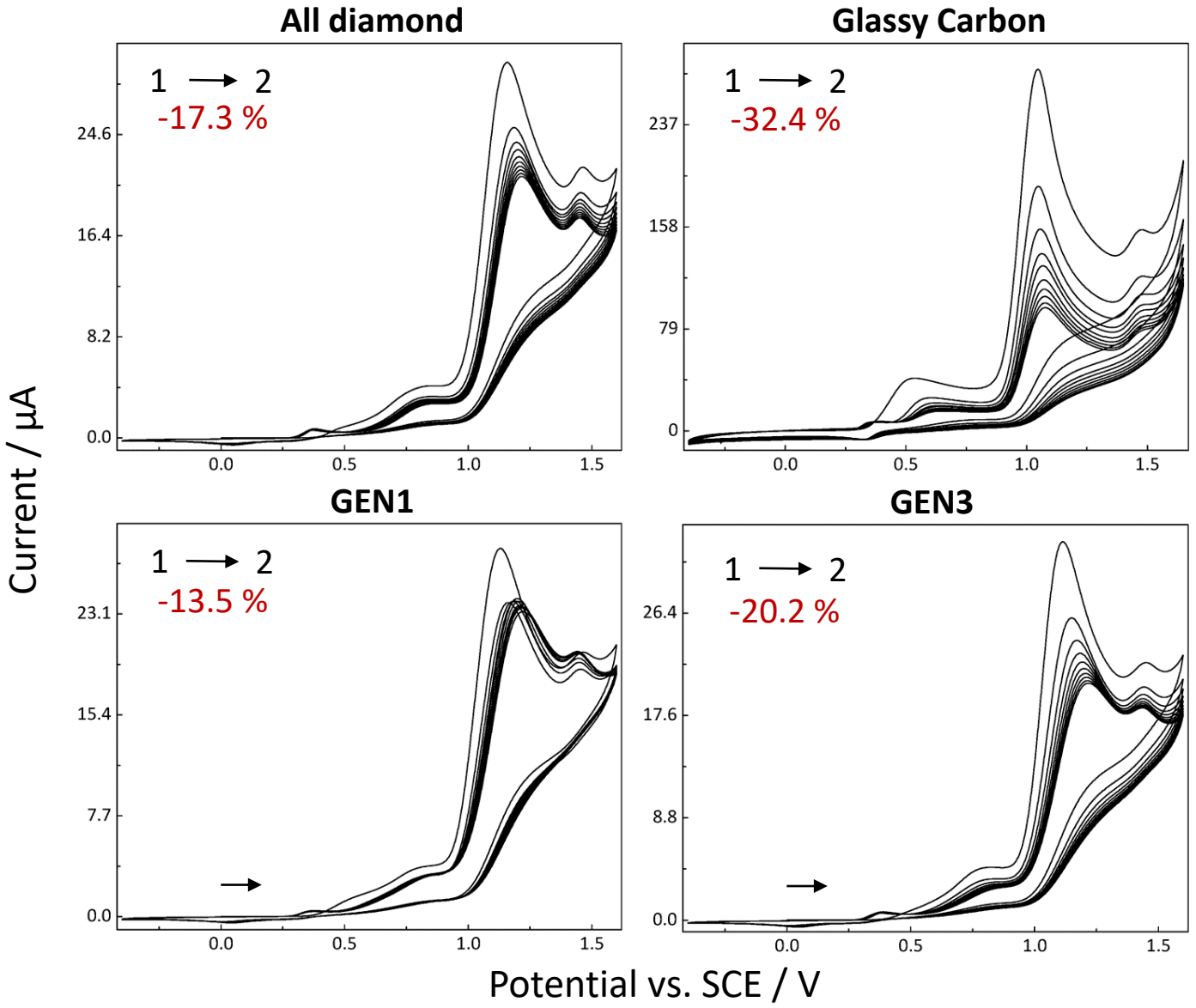

(a)
Reduction
Electrode
Solution
e^-
E_F
LUMO
Energy
E_F
HOMO
Applying negative potential
Electrode
Solution
LUMO
Potential
-
E_F
+
HOMO
Oxidation
(b)
Electrode
Solution
LUMO
Energy
E_F
e^-
HOMO
E_F
Applying positive potential

Capacitance and Solvent Windows



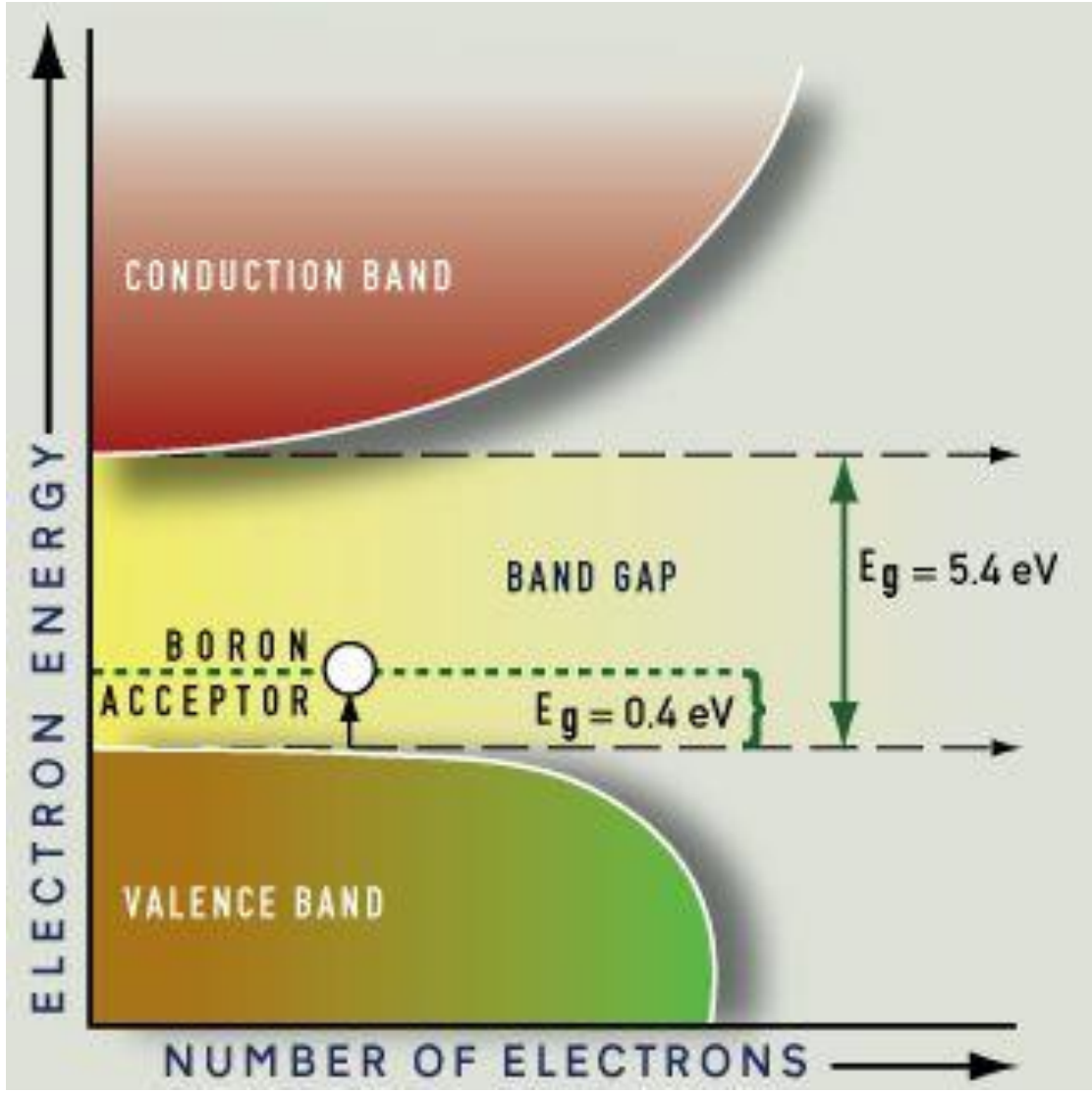
Capacitance and solvent window measurements using all diamond, GC, GEN1 and GEN3 electrodes.

Electrode Fouling in Synthetic Urine



- **Increased fouling** was observed compared to *in vitro* work on a simple blood model due to the **complex nature** of synthetic biological matrices
- Excluding GEN1, **increasing sp^2 content** resulted in **increased fouling**

CVs obtained of 1 mM APAP and 1 mM CAFF in synthetic urine (10 full scans).


CONDUCTION BAND
BAND GAP
$E_g = 5.4$ eV
BORON
ACCEPTOR
$E_g = 0.4$ eV
VALENCE BAND
ELECTRON ENERGY
NUMBER OF ELECTRONS