A new electrochemical device for multi-purpose screening

Jean-François Chateaux [1], Rainier-Numa Georges [2], Florian Bianco [1], Bastien Doumèche [2]*

[1] Univ Lyon, UCBL, INSA Lyon, ECL, CNRS, CPE Lyon, INL, UMR5270, Campus de la Doua, 6 rue Ada Byron, 69622 Villeurbanne, France
[2] Univ Lyon, UCBL, CNRS, UMR5246, ICBMS, 69622 Villeurbanne, France
* jean-francois.chateaux@univ-lyon1.fr

Electrochemistry is an universal detection method with the great advantage to be insensitive to optical interferences, the latter being the main drawback of most high-throughput screening methodologies. Unfortunately, electrochemical devices are not adapted to screen a large number of samples in a relative short time due to the lack of available device. In the CEITOP project, a 96-wells multipotentiostat was designed allowing to perform 96 electrochemical measurements in less than 1 second, also providing kinetic data for each well. The functioning of this new device is presented here illustrated by the detection of well-known redox probe used in enzyme inhibitor screening,

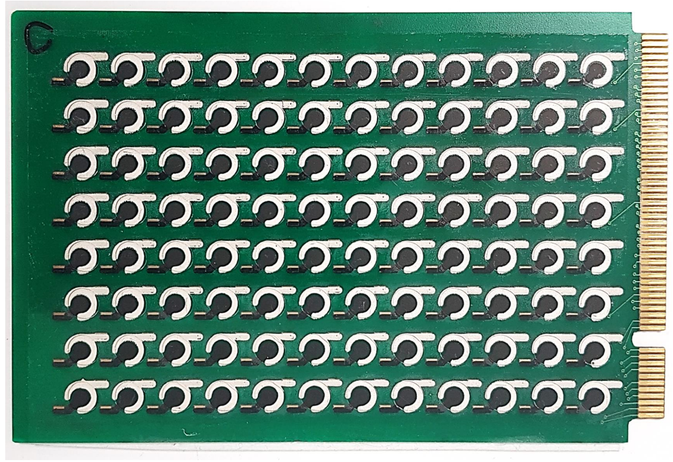


Fig. 1. Electrochemical experiments are performed on 96 multiplexed electrodes screen-printed on a PCB. Working electrodes are made of carbon and counter/ref are Ag|AgCl electrodes.

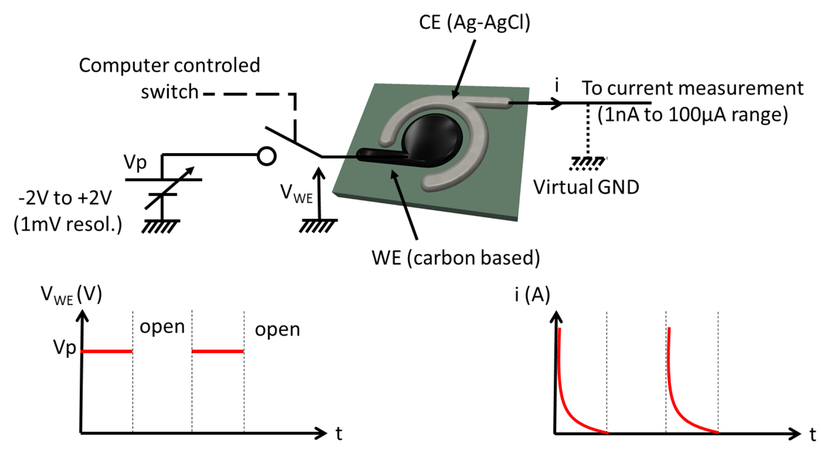


Fig. 2. Intermittent pulse amperometry (IPA) protocol : WE is switched from a polarized state to an open state periodically. During polarization, electrochemical current is measured.

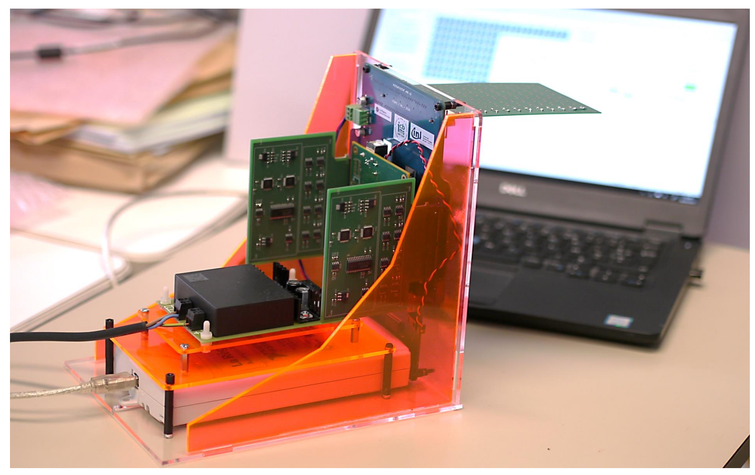


Fig. 3. New IPA device developed at Institut des Nanotechnologies de Lyon (INL). This instrument ensure high-speed multiplexing for each well polarisation and current measurement.

Acquisition parameters and User Interface

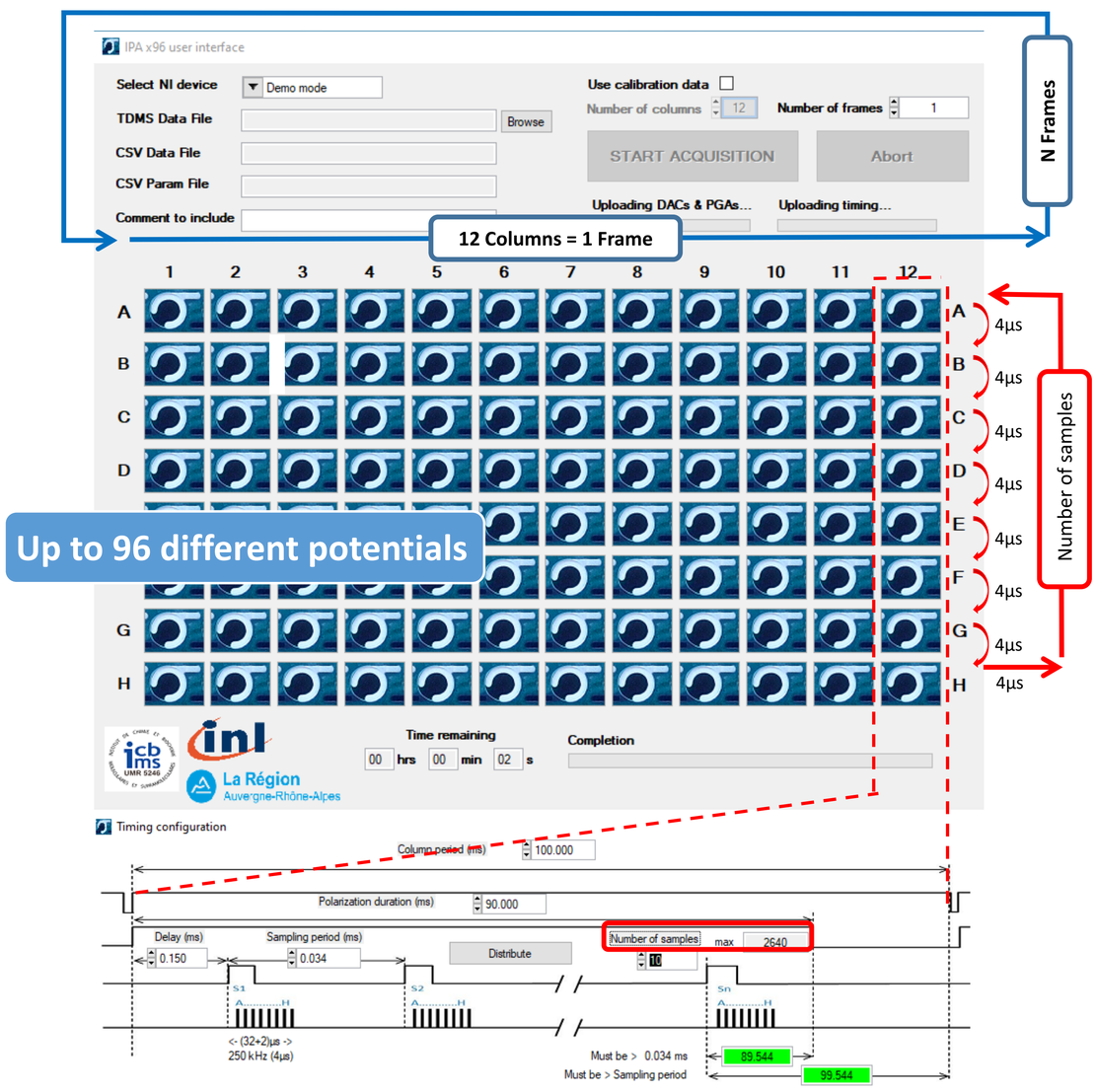


Fig. 4. User interface and multiplexing strategy.

- One frame consist of 96 chronoamperometric experiments that could be repeated indefinitely
- Measurements are made one column after the others.
- Each well in a given column receive a polarization pulse with its own amplitude value
- Polarization pulses duration can be ranged from microseconds (µs) to seconds (s)
- Current is measured in the range of 1 nA to 100 µA
- Sampling duration is 34 µs per column (wells A to H sampled almost simultaneously)
- Each well can be sampled at up to 30 kHz (4 Mb data flow)
- All samples are transfered in real time to the host computer for immediate display and further analysis (Cottrell fitting for example)

Electrochemical assays on a model system

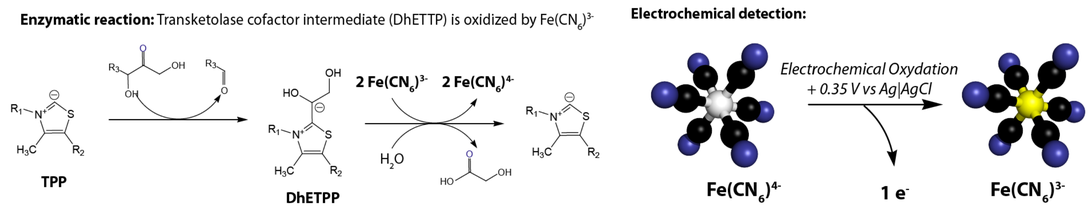
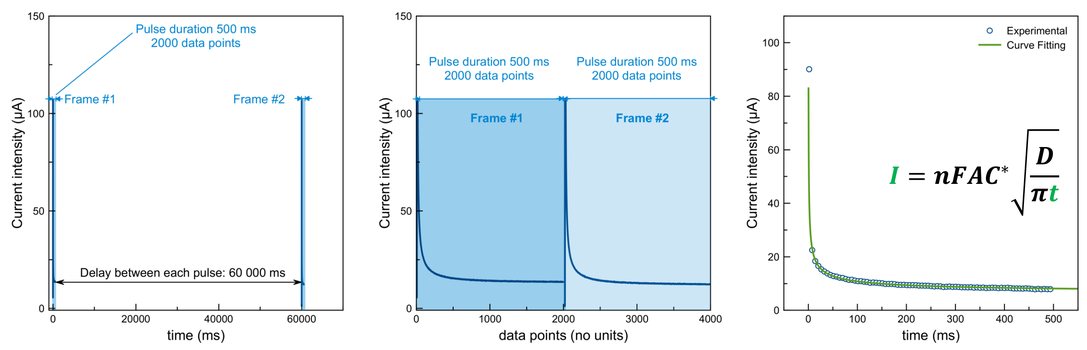
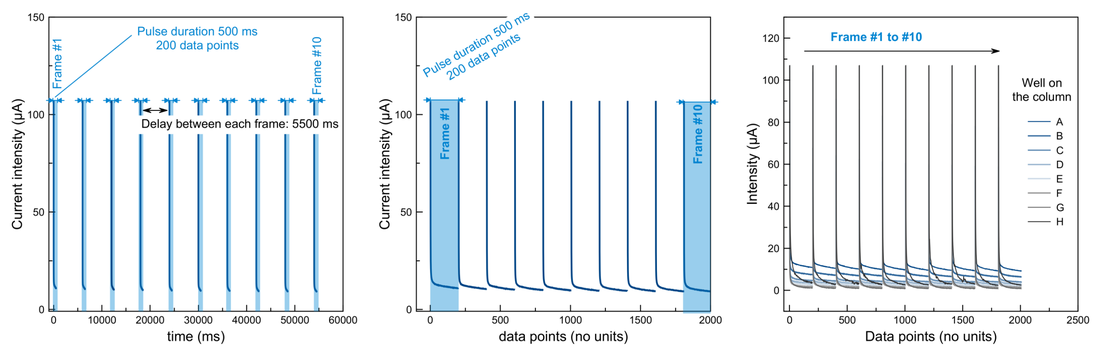


Fig. 5. Transketolases from pathogens are targeted enzymes to discover new antibiotics. A reaction intermediate (DhETTP) could be oxidized by $Fe(CN)_6^{3-}$ leading to $Fe(CN)_6^{4-}$ that could be detected electrochemically (see CEITOP Projet: ceitop.univ-lyon1.fr). Detection of $Fe(CN_6)_3^{4-}$ using the INL device highlights its adaptability to several electrochemical protocols. Two examples are shown to depict the IPA assay (on 1 and 8 wells for clarity).



Example #1: Potential is applied for 500 ms with one sample every 0.25 ms resulting in a I vs. t frame of 2000 data points. A second frame is acquired after 60 000 ms (1 min) (left). This protocol highlights that the electrical circuit is mostly opened during the experiment. The two frames are shown as function of data point number (middle) and as a first approximation, the I vs. t plot was fitted to the Cottrell equation (Only 80 points experimental points are shown for clarity) (right).



Example #2: Potential is applied for 500 ms with one sample every 2.5 ms resulting in a I vs. t frame of 200 data points. Ten frames are acquired during 60 000 ms (1 min) (left). All frames results in nearly identical I vs. t curves (middle). Variability still occurs due to non-optimized screen-printing (right) (*work in progress*).

The new instrument developed by INL in close collaboration with ICBMS gives the ability to perform rapidly numerous **Intermittent Pulse Amperometry (IPA)** assays with high sensitivity (down to nA range) thanks to the architecture of 96 multiplexed electrodes. All 96 experiments can be different regarding the polarization potential and current measurement range. The access to all raw data allows to perform data post-treatment. Because this IPA instrument allows to detect rapidly current intensity variations at numerous different potentials on several electrodes, it's also possible to obtain a voltammetry like profile and to determine the oxidation or reduction potential for a given species.
Among all electrochemical methods, IPA could be applied for biomedical and pharmacological projects. With the possibility of multiplexing it becomes possible to assay a large set of molecules from chemical libraries in a reasonable time [1, 2].

[1] Abdellaoui, S. *et al*. A 96-well electrochemical method for the screening of enzymatic activities, Analytical chemistry, 2013, DOI: /10.1021/ac303777r
[2] Aymard CMG *et al*, Analytical Chemistry, 2018, DOI: 10.1021/acs.analchem.8b01752

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