

**Electronic Supplementary Information for Analyst**

**Electrically Wired Mitochondrial Electrodes for Measuring Mitochondrial Function for Drug Screening**

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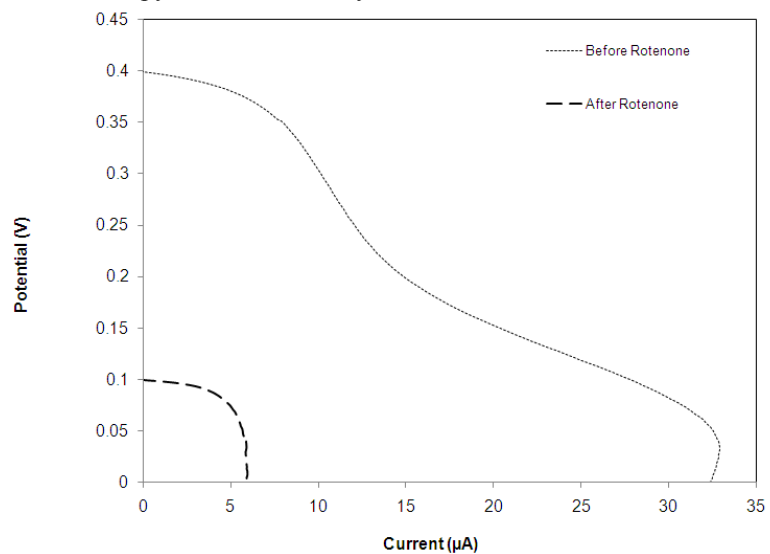
**Supplementary Data Discussion:**

Half cell current measurements were completed by generating polarization curves in a three electrode setup that used a platinum mesh counter electrode separated from the running solution with a Nafion<sup>®</sup> membrane salt bridge, an Ag/AgCl reference electrode, and a mitochondrial working electrode. Representative polarization curves are shown in Figures S1 and S2 for mitochondrial and blank electrodes, respectively. After spiking of the solution with rotenone to 500nM, the currents and potentials for the mitochondrial electrodes dropped substantially. The blank electrodes did not change dramatically after the addition of rotenone and had several orders of magnitude less current compared to the mitochondrial electrodes. The results from these experiments are tabulated in Table S1.

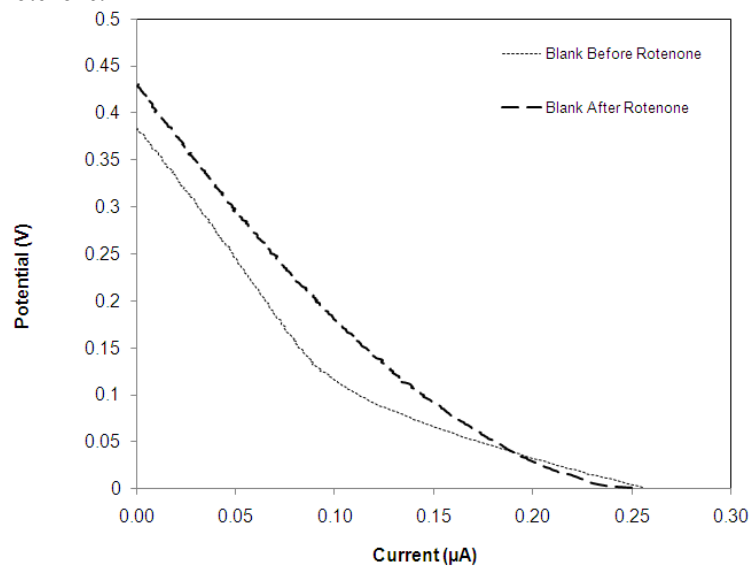
The effect of dissolved oxygen concentration on the currents of the mitochondrial electrodes was examined by running normal mitochondrial electrodes in degassed, aerated, and oxygenated solutions. The current to oxygen concentration is correlated in Figure S3. The R<sup>2</sup> value for the data is 0.9826 and shows linear oxygen concentration dependency which is in agreement with the concept that there is a competition for the electrons by complex IV when oxygen is present.

### Supplementary Figures

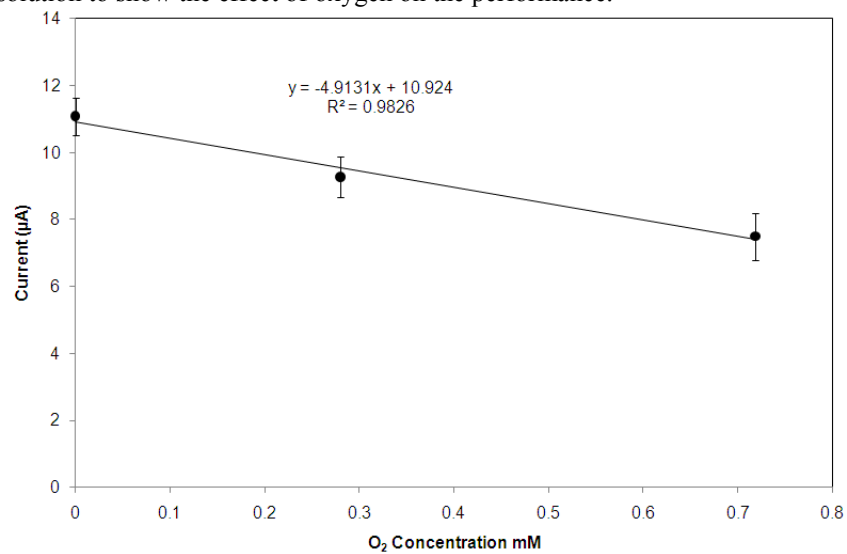
**FigureS1:** Representative polarization curves with the reference potential subtracted for mitochondrial electrodes incubated in pyruvate followed by treatment with 500nM rotenone.



**Figure S2:** Representative polarization curves with the reference potential subtracted for blank electrodes (electrodes containing no immobilized mitochondria) incubated in pyruvate followed by treatment with 500nM rotenone.



**FigureS3:** Comparison a mitochondrial electrode operated in degassed solution, aerated solution, and oxygenated solution to show the effect of oxygen on the performance.



**Supplementary Table**

**Table S1:** Comparison of average potential and maximum current before and after rotenone addition with a mitochondrial electrode, and a blank that contains no mitochondria.

Experiment	Current (Amps)	Current (Amps) After Rotenone	Potential (mV) Before Rotenone	Potential (mV) After Rotenone
Mitochondria	$3.10 \times 10^{-5} \pm 0.72$	$7.94 \times 10^{-6} \pm 1.69$	387±15	117±18
Blank	$1.95 \times 10^{-7} \pm 1.02$	$1.59 \times 10^{-7} \pm 1.16$	369±70	347±90