The Use of Copper-Based MOFs in Creatinine Detection

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Monitoring kidney function over time is crucial for determining the proper care of kidney disease patients. Kidney health is assessed by measuring creatinine, a waste product of muscle metabolism that displays a strong positive correlation between its concentration in the bloodstream and kidney function decline. Current techniques for measuring creatinine, such as blood tests and MRIs, are time-intensive and must be conducted by professionals. We are currently developing an electrochemical biosensor for continuous creatinine monitoring in interstitial fluid (ISF) as a cost-effective, user-friendly solution. The sensor uses copper as the biorecognition element for creatinine detection. Cyclic voltammetry (CV) study revealed copper's capability to form a spontaneous complex with creatinine. We previously confirmed this complex formation by electrochemically detecting creatinine with a copper-coated carbon electrode through cyclic voltammetry (CV) in DI water with varying creatinine concentrations. Two oxidative peaks were observed, the first corresponding to free copper ions in solution and the second to the copper-creatinine complexes. Increased separation between peaks with higher creatinine concentrations demonstrated their spontaneous formation. A calibration curve from the CV data shows a linear relationship between creatinine concentration and peak separation. We are now developing a copper-based metal-organic framework (MOF) to help prevent interference from contaminants in ISF, improving the specificity of copper as our sensing agent. MOFs are highly selective structures made of metal nodes and organic ligands that can form porous, nano-scale 2D and 3D shapes. Our system is comprised of Cu-TCPP nanosheets synthesized using a solvothermal reaction of $Cu(NO_3)_2$, 5,10,15,20-tetrakis(4-carboxyphenyl)porphyrin (H2TCPP), and a solvent mixture. These nanosheets are stamped on top of one another to form films on different substrates that can then be tested through CV to determine the detection capabilities of the MOF.

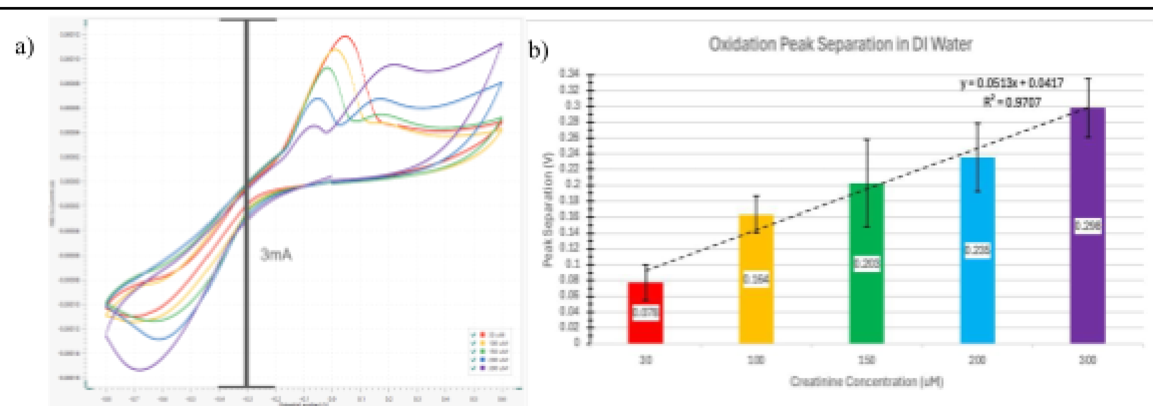

*Figure 1. **(a)** Results of CV performed on carbon electrodes with Cu-deposited surface in DI water with varying concentrations of creatinine. **(b)** Linear calibration curve generated*

based on the separation between potentials of each oxidative peak occurrence ($y=0.0513x + 0.0417$, $R^2=0.9707$).

Draft Work

1. General biosensing, kidney disease, relation of creatinine to kidney health: Lauren
   Chronic Kidney Disease (CKD), a progressive and potentially fatal condition, affects over 10% of the world population and has emerged as one of the leading causes of death worldwide. CKD largely affects older individuals, and has a large prevalence in middle and low-income countries where treatments and testing procedures are not widely available or affordable. This condition refers to the gradual loss of kidney function, which filters waste and excess fluids from the bloodstream. One of these waste products includes creatinine, a molecule produced by muscle metabolism and displays a strong correlation between its increasing concentration in the bloodstream and CKD progression. Therefore, many current technologies for tracking the progression of CKD rely upon the detection of creatinine concentration in the patient's bloodstream or serum. However, while many of these techniques, such as ultrasounds, MRIs, x-rays, CT scans, or blood tests, are extremely accurate, they are also expensive, time-intensive, and require trained professionals. As a result, researchers are moving towards biosensors, which present a cheap, user-friendly way to establish regular monitoring of creatinine to catch progression in CKD before major complications arise. Our electrochemical biosensor aims to detect creatinine concentration continuously in interstitial skin fluid by utilizing the natural formation of copper-creatinine complexes.
2. Creatinines molecular structure, complex formed, detection with copper: Lily

Creatinine is a heterocyclic organic compound that is derived from creatine metabolism with the chemical formula of $C_4H_7N_3O$, and its 5 membered ring structure makes it highly soluble in water. This allows it to circulate freely in the bloodstream and be excreted by the kidneys without significant reabsorption or secretion. This property makes creatinine an effective biomarker for kidney function. When reacting with transition metals, creatinine acts as a ligand. It forms coordination complexes through its nitrogen and oxygen atoms. Transition metals such as copper, zinc, and nickel, have vacant d orbitals, and this enables them to bind with electron donating atoms in creatinine, typically nitrogen and oxygen, to stabilize metal- ligand interactions. These metal-creatinine complexes show distinct electrochemical properties, which can be utilized for biosensing applications. The selective binding of creatinine to transition metal allows for electrochemical detection by tracking shifts in oxidation potential or current response to determine its concentration.

Our previous work focused on the electrochemical detection of creatinine using a carbon electrode with deposited copper. Cyclic Voltammetry (CV) was conducted in DI water with varying concentrations of creatinine. Two oxidative peaks were observed. The first one corresponds to free copper ions released into solution and the other one to the copper creatinine complexes. As the creatinine concentration increased, the peak separation also increased, and this indicates that creatinine binds to copper, altering the oxidation potential. A calibration curve also showed a linear relationship between creatinine concentration and peak separation, which shows that copper can be used to electrochemically track creatinine complex formation.

3. What MOF is, why MOF, plan for MOF synthesis: Charlie
   Knowing that copper and creatinine form a unique covalent complex allows for the more specific application of this concept using metal organic frameworks, or MOFs. MOFs are structures composed of metal nodes linked together by organic ligands. These crystalline compounds form porous structures on the nano-scale that can be synthesized in a 2D or 3D manner. Due to their porous nature, MOFs show promise in the world of biosensing as they have high adsorption capacities for biomolecules, and can additionally be tuned to have increased selectivity for specific molecules. Our system is comprised of Cu-TCPP nanosheets that were synthesized using a solvothermal reaction of Cu(NO3)2, 3H2O and 5,10,15,20-tetrakis(4-carboxyphenyl)porphyrin (H2TCPP) in a mixture of N,N-diethylformamide and ethanol. These nanosheets can then be stamped on top of one another to form films of desired thickness on different substrates. By stamping these nanosheets on a gold-plated, laser-induced graphene electrode, we can construct a continuous sensor capable of monitoring creatinine levels in interstitial skin fluid.