Polypeptides synthesis through electrochemical oxidation of thioglycine<quillbot-extension-portal></quillbot-extension-portal>

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Polypeptides play an important role in the emergence of life in prebiotic chemistry, acting as catalysts, enzymes, and self-replicating molecules. In the ocean and deep-sea environments where dehydration reaction to form peptides are less plausible, the polymerization of aminothioacids can be a potential mechanism for the formation of peptides, using metal ions as oxidants to promote reaction [1–3]. Because there is an electrochemical potential on the deep-sea hydrothermal vent [4], we anticipated that electrochemical oxidation of the aminothioacids can be considered as one of the effective polymerization pathways. In our study, we investigated the electrical polymerization of the thioacid form of glycine, known as thioglycine (Gly-SH) for synthesizing polypeptides in aqueous environments.
We performed our experiment in an electrochemical cell (Figure 1) that consisted of a gold working electrode (WE), a platinum counter electrode (CE), and an Ag/AgCl reference electrode (RE). The electrolysis was performed by applying a continuous current at +1.1 V oxidation potential for two days during slowly adding an aqueous solution of thioglycine (0.1 M, 10 mL / 100 min) into the gold working electrode side containing 50 mL of 0.5 M H_3PO_4 electrolyte (pH 1.5). During the electrolysis, 1 mL of the reaction mixture was sampled periodically for HPLC analysis and recorded the pH.
During the electrolysis, the colorless transparent solution turned into yellow turbid, accompanied by an increase in current, indicating oxidation of Gly-SH. The HPLC analysis showed that diglycine was the most abundant and polypeptides up to hexaglycine were identified. The concentration of the polypeptides increased with the electrolysis period, reaching a maximum after 12 hours. The polymerization reaction did not proceed at all without electrolysis.
The possible reaction mechanism of polymerization of thioglycine involves electrochemical oxidation of Gly-SH on the anode, generating a thioester (-C(=O)S-) intermediate. This intermediate then rearranges to form a dipeptide having an amide bond (-C(=O)-NH-) and thioacid C-terminal. The thiol can be either hydrolyzed to form peptides or re-oxidized for further polymerization with another thioglycine to form a tripeptide and longer peptides.
Overall, our study demonstrates the potential of thioglycine oligomerization via electrochemical reactions as a mechanism for polypeptides synthesis. The results of this study support the idea that electrochemical reactions may have played a significant role in the formation of biologically relevant molecules in the early Earth's environment. However, further research is needed to fully understand the potential of this process and how it may have contributed to the origin of life on the early Earth.

References:
1. Liu, R., & Orgel, L. E. *Nature*, 389(6646), 52–54.(1997).
2. Maurel, M.-C., and Orgel, L. E. *Orig. Life Evol. Biosph.* 30, 423–430. (2000).
3. Okamoto, R. et al. *Biochemistry*, 58(12), 1672–1678. (2019).
4. Yamamoto, M. et al. *Angew. Chem. Int. Ed.* 56, 5725–5728 (2017).
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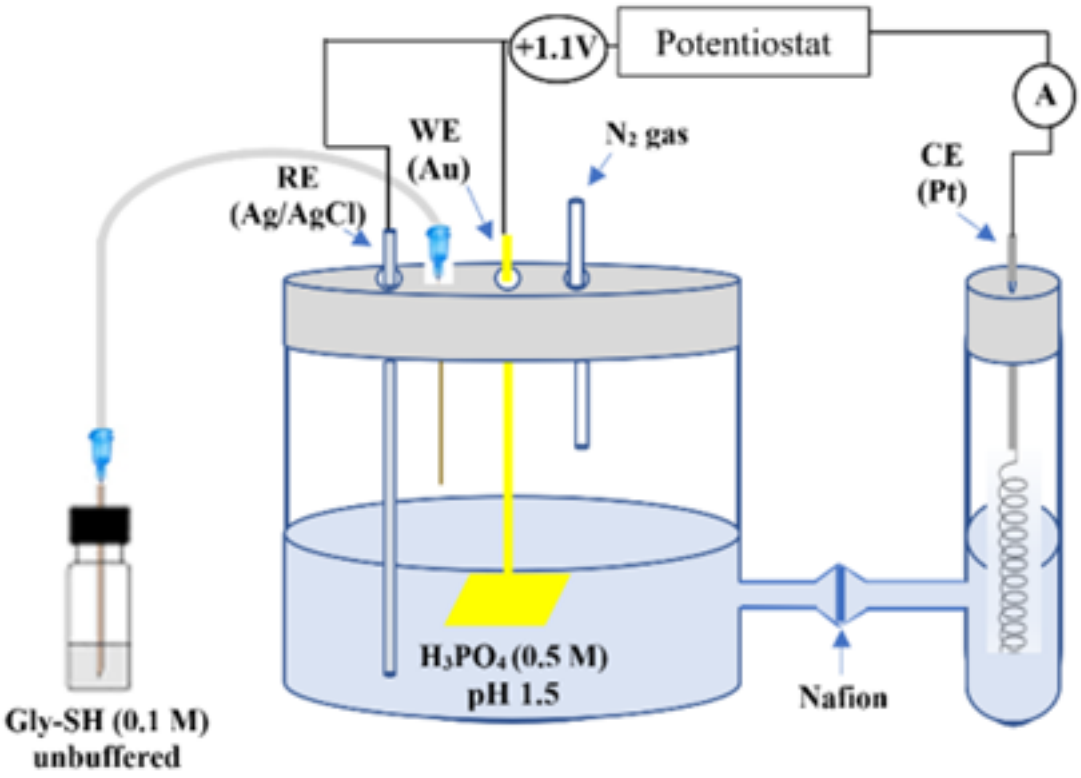

Figure 1. Gly-SH oxidative polymerization in an electrochemical cell

