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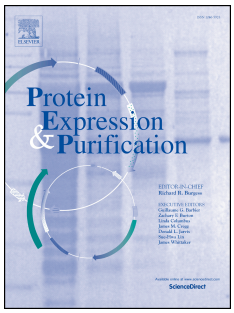

A multi-column plate adapter provides an economical and versatile high-throughput protein purification system

Matthew J. Dominguez, Benjamin J. Lantz, Rebecca J. Rhode, Zoey L. Sharp, Krysten C. Finney, Valeria Jaramillo Martinez, Elliott J. Stolla

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Abstract

Protein purification is essential in the study of protein structure and function, and the development of novel therapeutics. Many studies require purifying multiple proteins at once, increasing the demand for improved purification methods. We hypothesized that multiple chromatography columns could be interfaced with a multi-well collection plate for rapid and convenient protein purification without the need of expensive instrumentation. As such, we developed a multi-column plate adapter (MCPA), which provides an economical yet versatile and time efficient, high-throughput protein purification system. The MCPA system simultaneously purified milligrams of different proteins under gravity or under vacuum for faster purification. The MCPA handles up to twenty-four 12 mL columns and multiple MCPA's in sequence allow milligram-scale purification of 96 different samples with relative ease. We also used the MCPA system for large scale affinity purification of four proteins, providing sufficient yields and purity for protein crystallization and biophysical characterization. The MCPA system is ideal for optimizing resin type and volume or any other purification parameter by customizing individual columns during the same purification. The high-throughput and versatile nature of this system should prove to be useful in obtaining adequate amounts of protein for subsequent analyses in any laboratory setting.

Introduction

Protein purification is an ever-important method for both academia and industry, [1, 2] as protein-ligand structural analysis is central to biochemistry and the drug discovery process [3, 4]. Production of relevant target proteins can become a bottleneck as the main biophysical techniques used to investigate structure, x-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, require milligrams of high purity protein [5-7]. The advancements of cryo-electron microscopy (cryo-EM) can allow for structural determination with relatively less protein, [8, 9] but the basic need to quickly and effectively purify protein remains. Recombinant protein purification with affinity chromatography, specifically immobilized metal affinity chromatography (IMAC), is one of the most efficient techniques to achieve high purity and yields [10, 11]. The versatile and widespread use of IMAC has led to the development of high-throughput technologies to rapidly purify many samples [2, 12]. Most high-throughput protein purification (HTPP) IMAC methods involve automated systems with costly instruments and commercial kits [4].