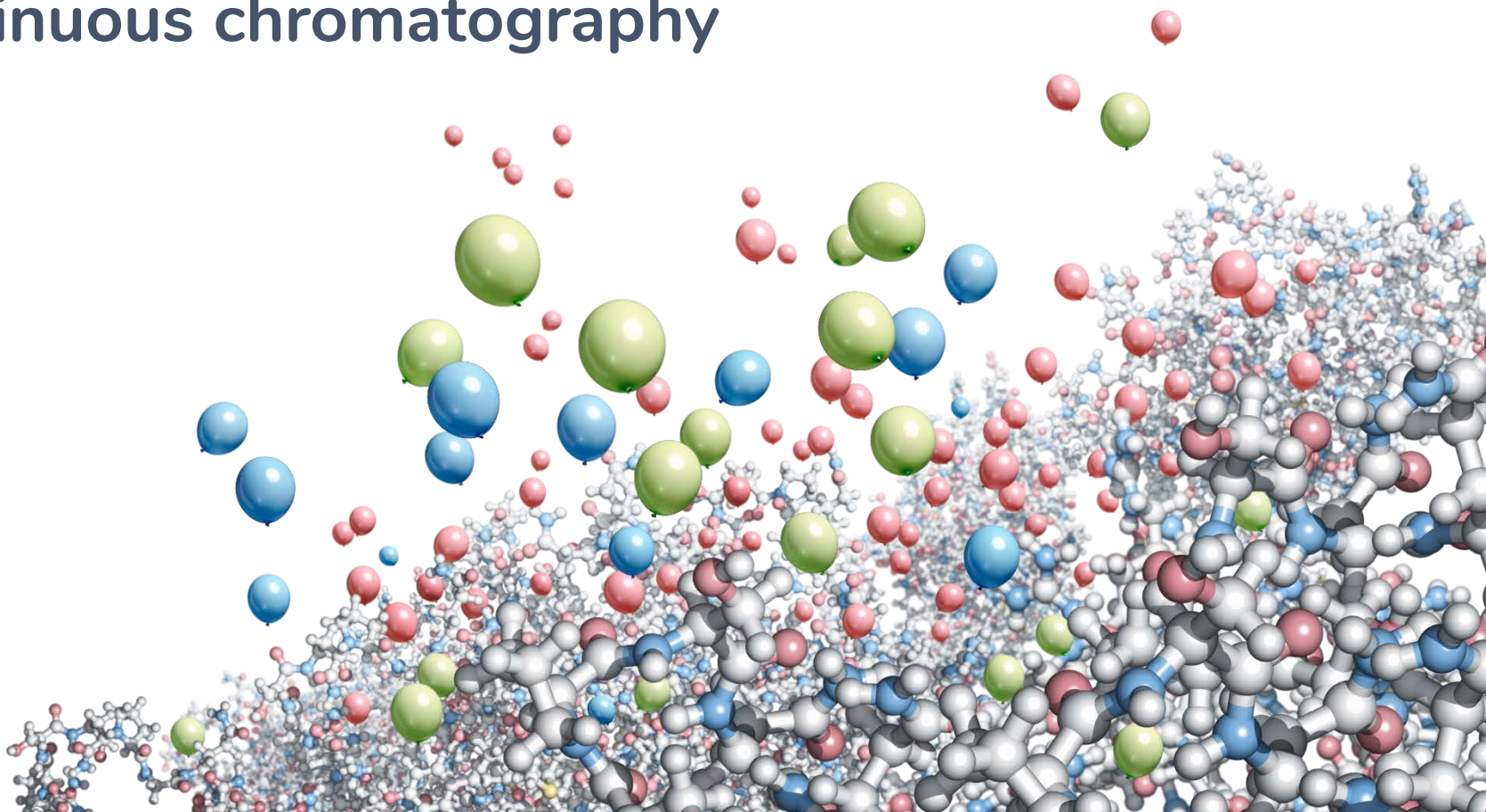


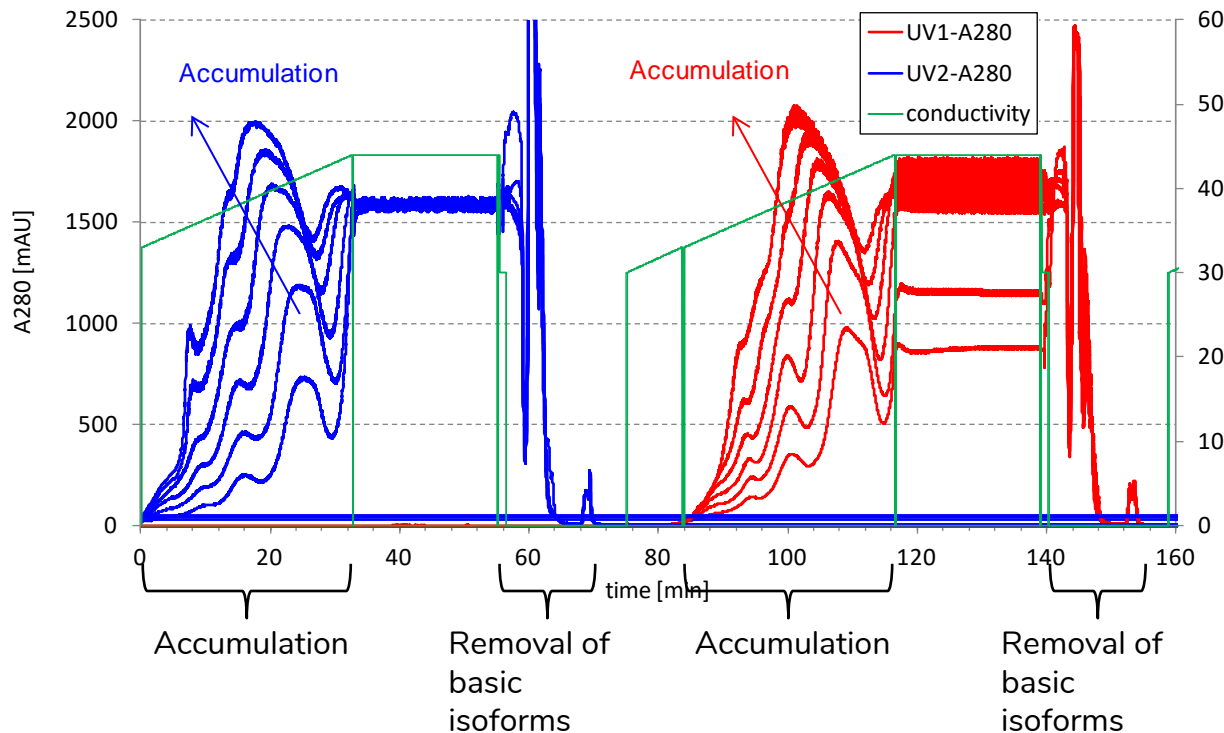
# The N-Rich process principle

Enriching minor components by  
continuous chromatography



# N-Rich uses

- Invaluable tool for development ICH-Q3A(R2) impurity isolation and characterization
- Proven for difficult to isolate biosimilar isoforms / product-related impurities
- Automated proteome/metabolome screening



Example:  
Enrichment of acidic  
mAb isoforms from  
cycle to cycle using  
N-Rich

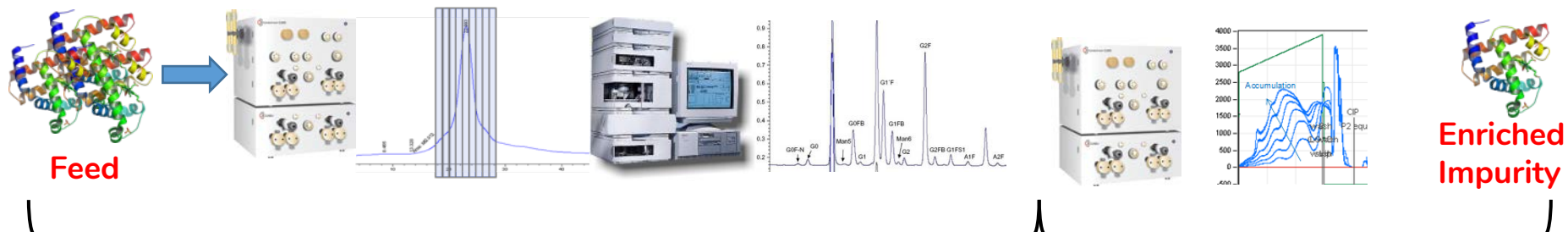


# N-Rich concept

Prep. batch  
Contichrom

Analytics  
UPLC

N-Rich  
Contichrom



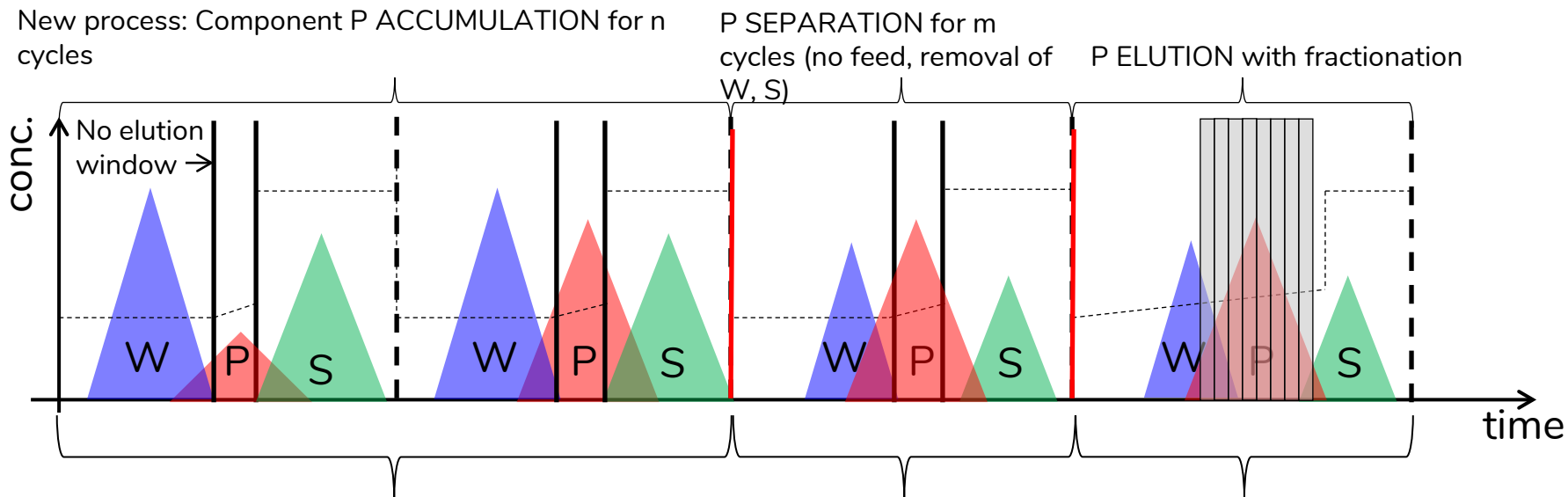
**STEP 1:** Preparative batch separation with Contichrom and UPLC analysis of fractions to identify fractions containing the desired compound

**STEP 2:** Automatic overnight execution of N-Rich to enrich and isolate compound of interest

- ✓ avoids tedious collection of prep fractions
- ✓ N-Rich single run to enrich side components AND deplete undesired main component overnight
- ✓ High throughput, save weeks of tedious repetitive work
- ✓ Preserve integrity of isolated impurity

# N-Rich compound enrichment process concept

- Process scheme:



## Accumulation

Increase concentration of P, absolute and relative to W and S.

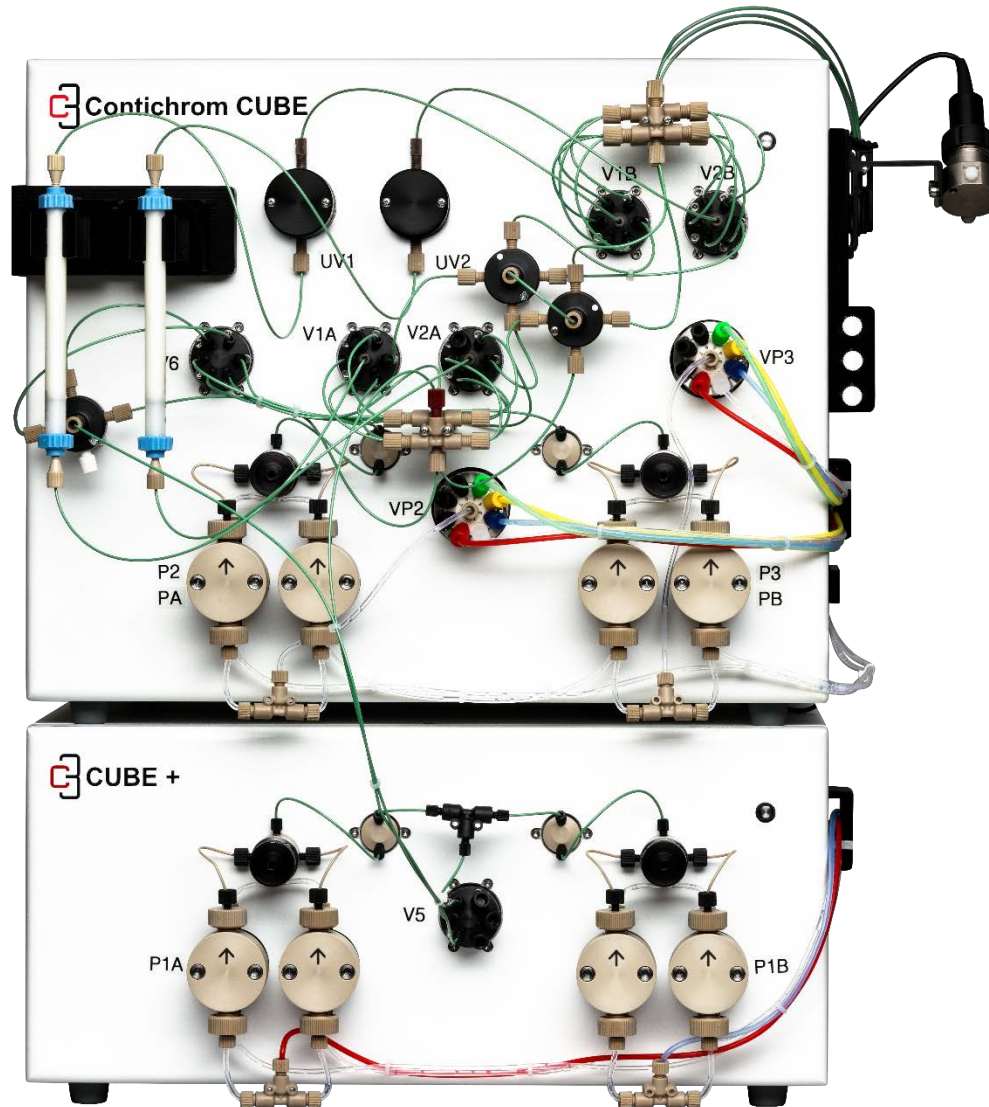
## Separation

Increase conc. of P, absolute and relative to W and S. Different gradient possible.

## Elution

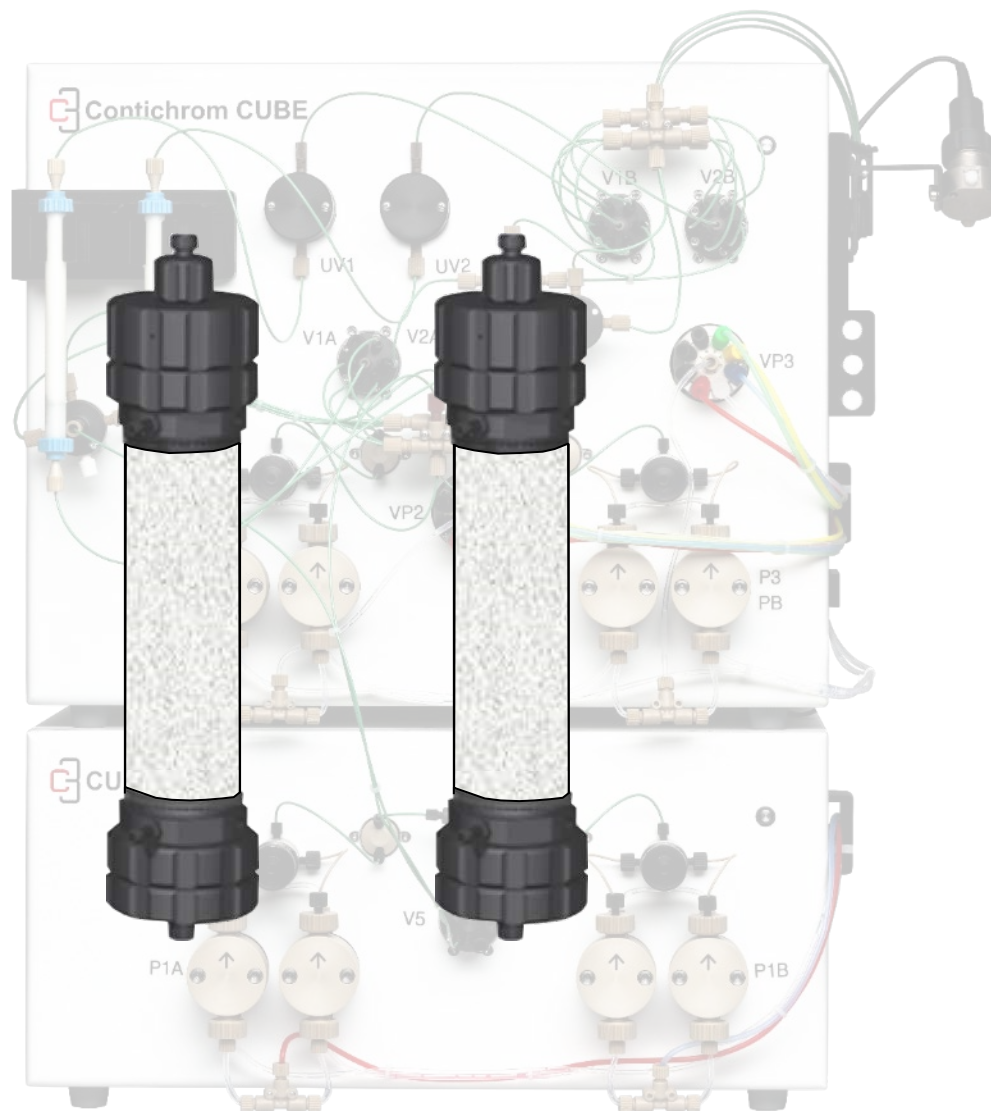
Final elution with shallow gradient and fine fractionation.

# Contichrom and N-Rich explained

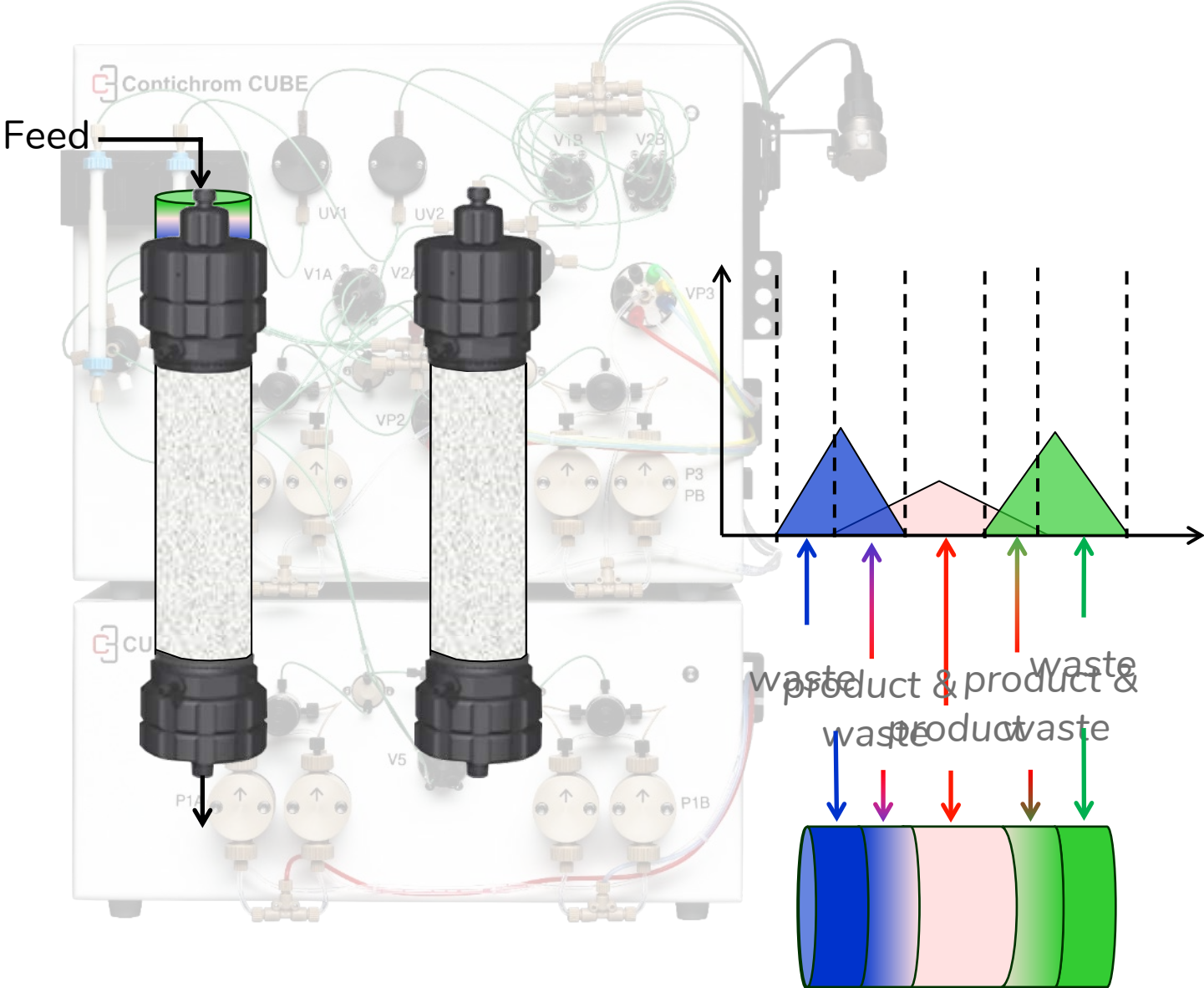




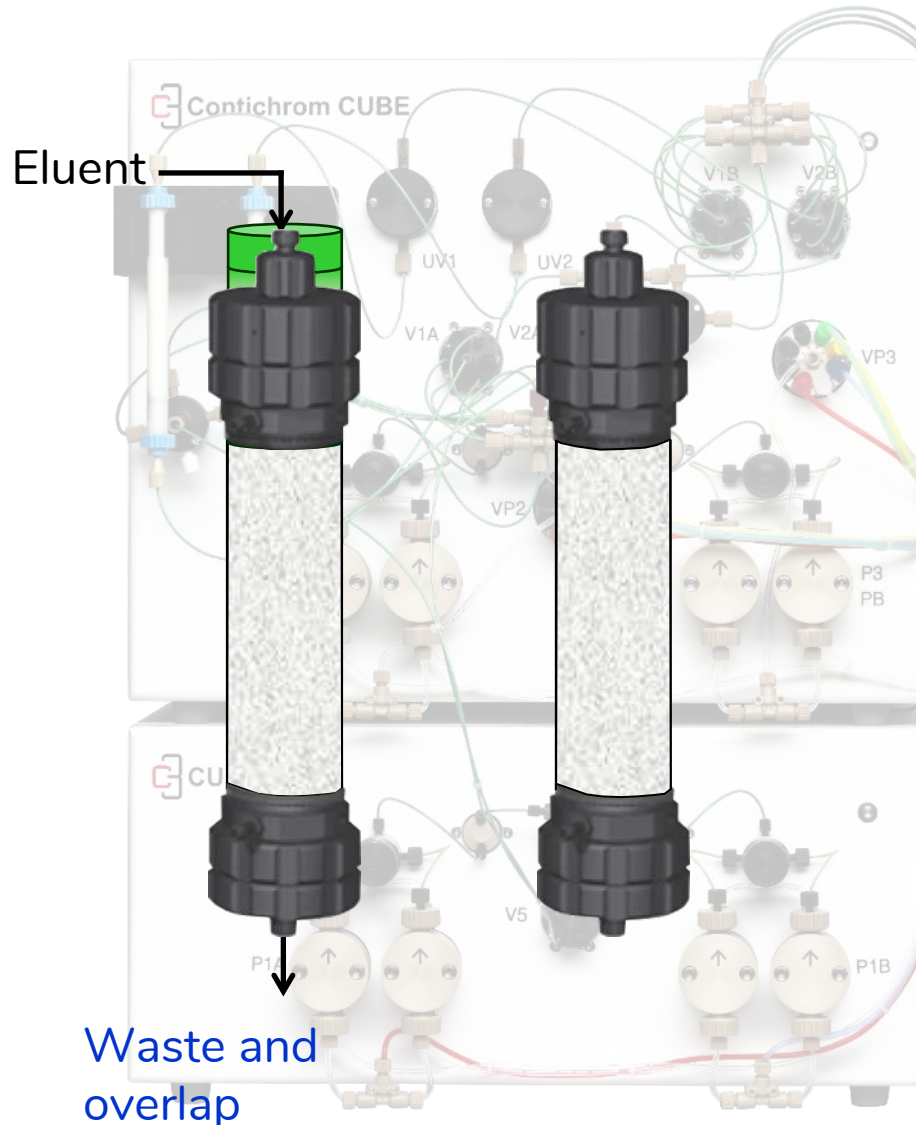
# Contichrom and N-Rich explained



# Contichrom and N-Rich explained



# Contichrom and N-Rich explained



## Step 1:

- feed column
- elute waste

## Step 2:

- recycle product

## Step 3:

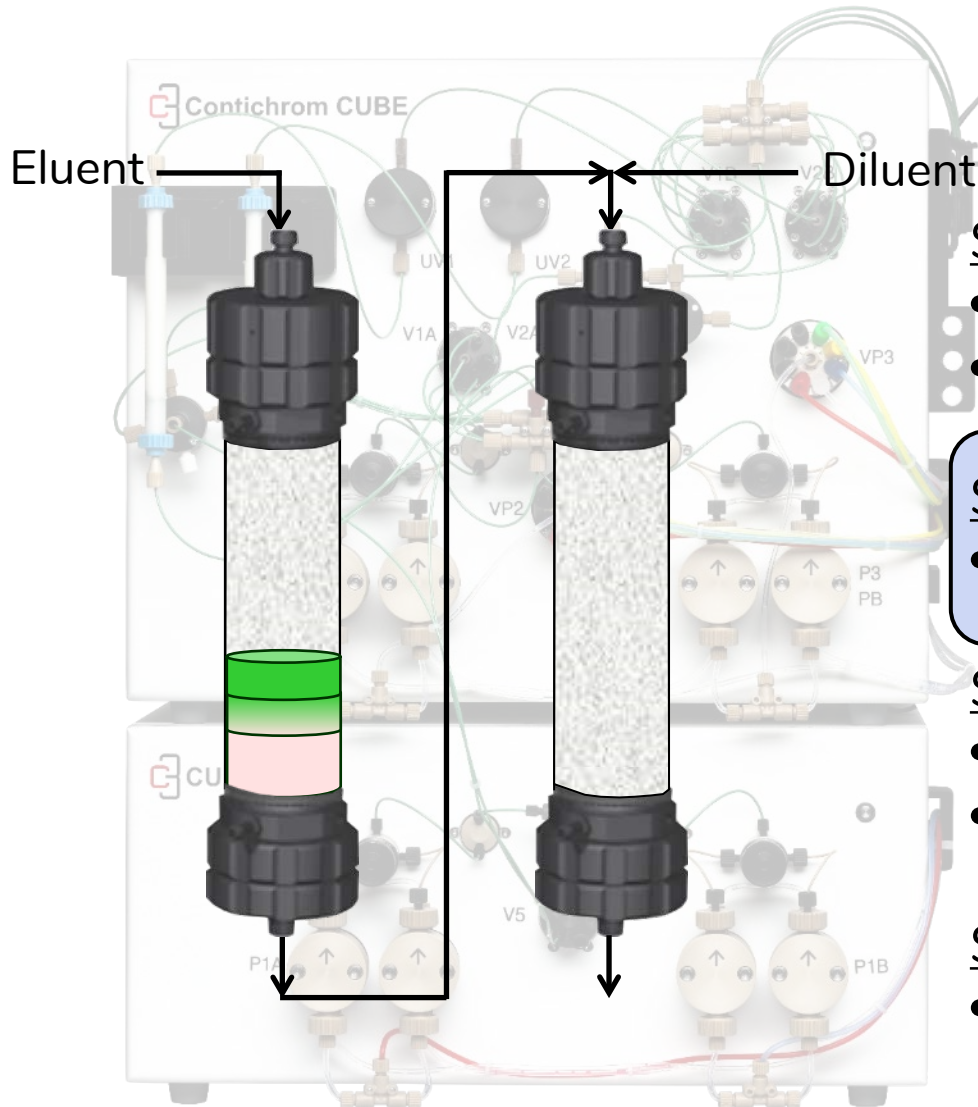
- feed column
- elute waste

## Step 4:

- recycle product



# Contichrom and N-Rich explained



## Step 1:

- feed column
- elute waste

## Step 2:

- recycle product

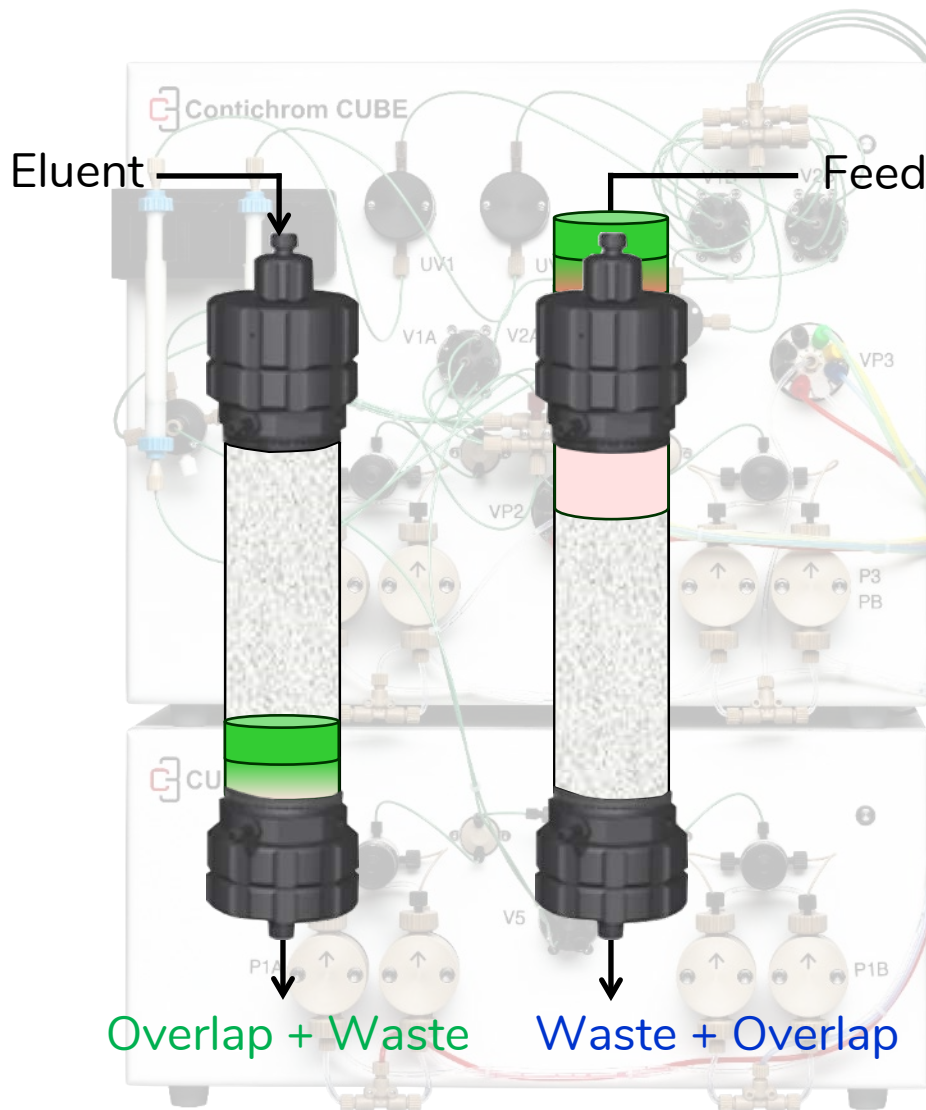
## Step 3:

- feed column
- elute waste

## Step 4:

- recycle product

# Contichrom and N-Rich explained



## Step 1:

- feed column
- elute waste

## Step 2:

- recycle product

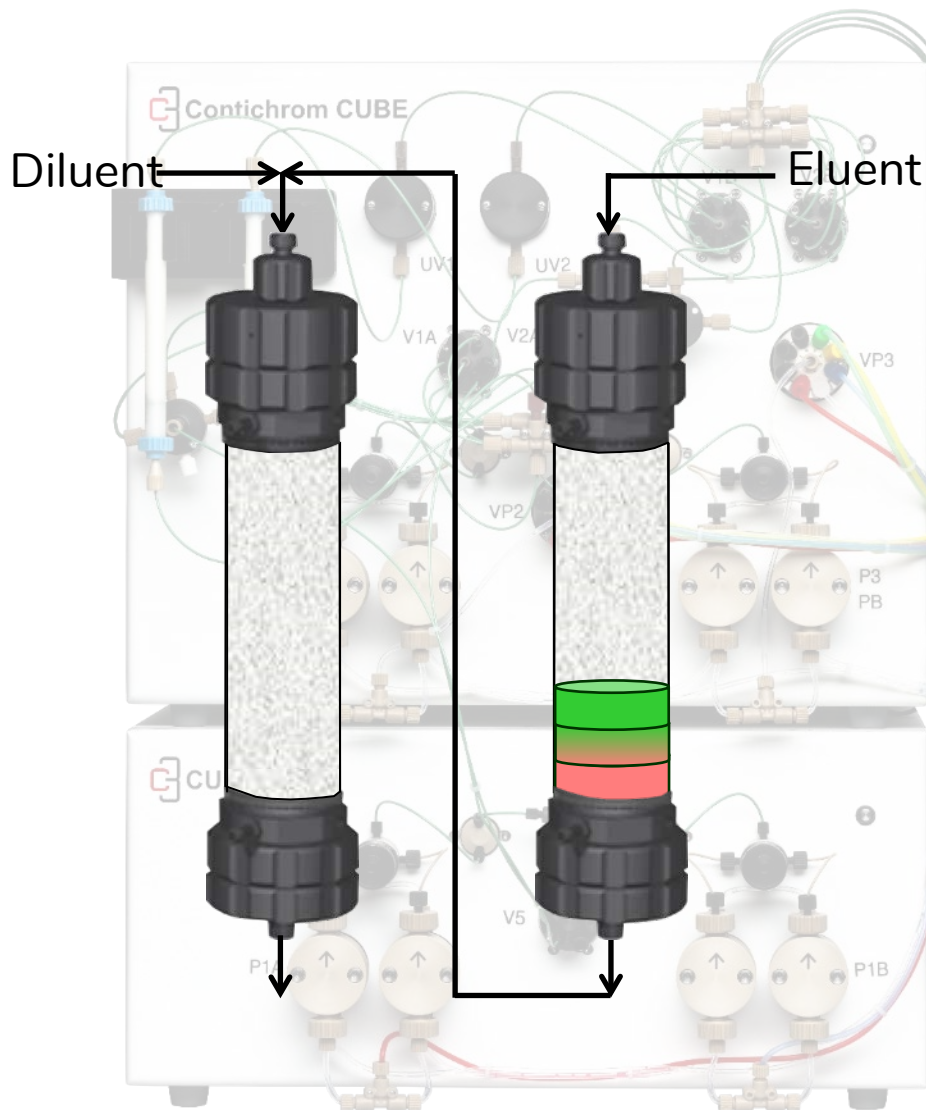
## Step 3:

- feed column
- elute waste

## Step 4:

- recycle product

# Contichrom and N-Rich explained



## Step 1:

- feed column
- elute waste

## Step 2:

- recycle product

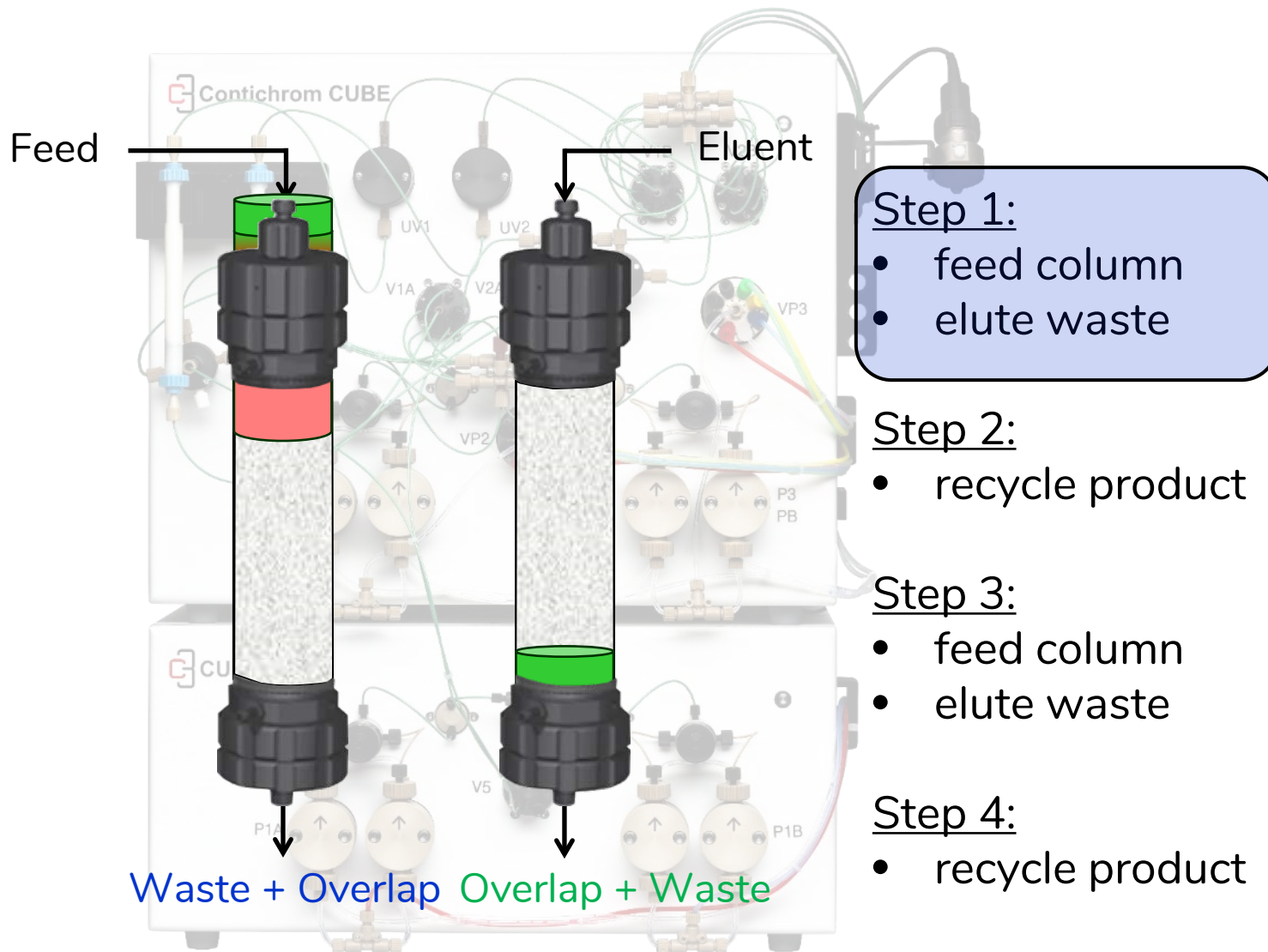
## Step 3:

- feed column
- elute waste

## Step 4:

- recycle product

# Contichrom and N-Rich explained



## Step 1:

- feed column
- elute waste

## Step 2:

- recycle product

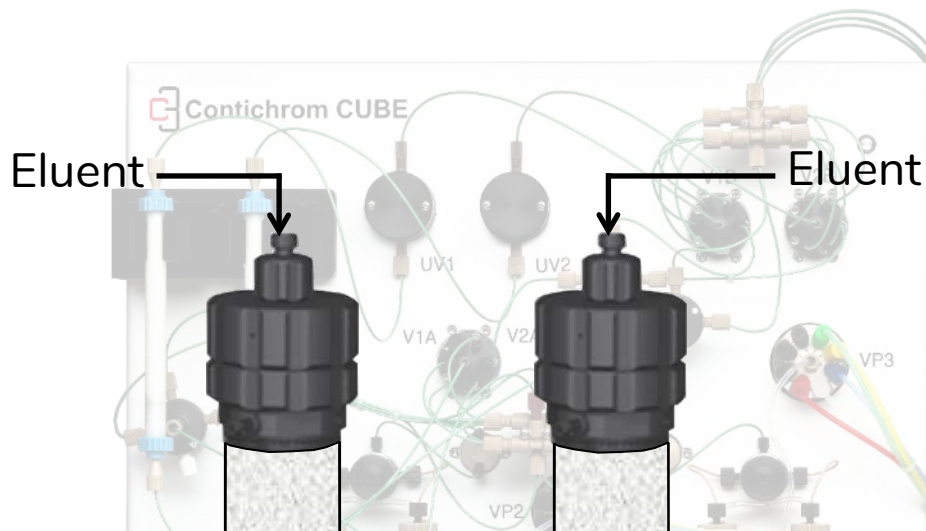
## Step 3:

- feed column
- elute waste

## Step 4:

- recycle product

# Contichrom and N-Rich explained



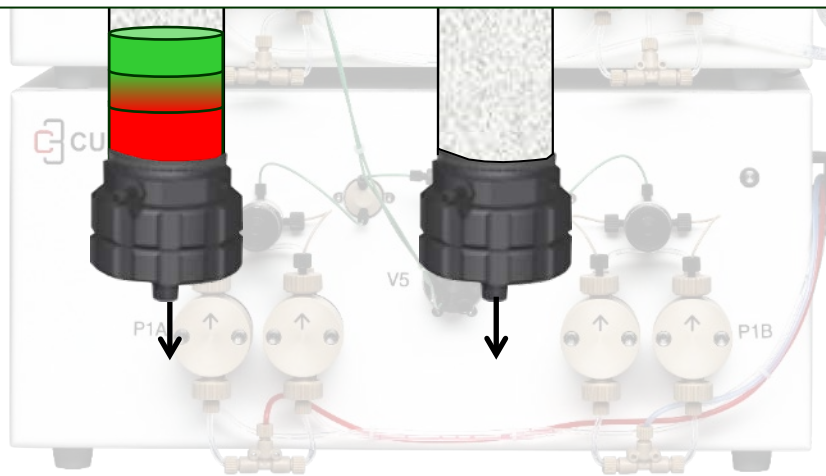
Step 1:

- feed column
- elute waste

Step 2:

recycle product

**Cycle complete , start next cycle**



Step 3:

- feed column
- elute waste

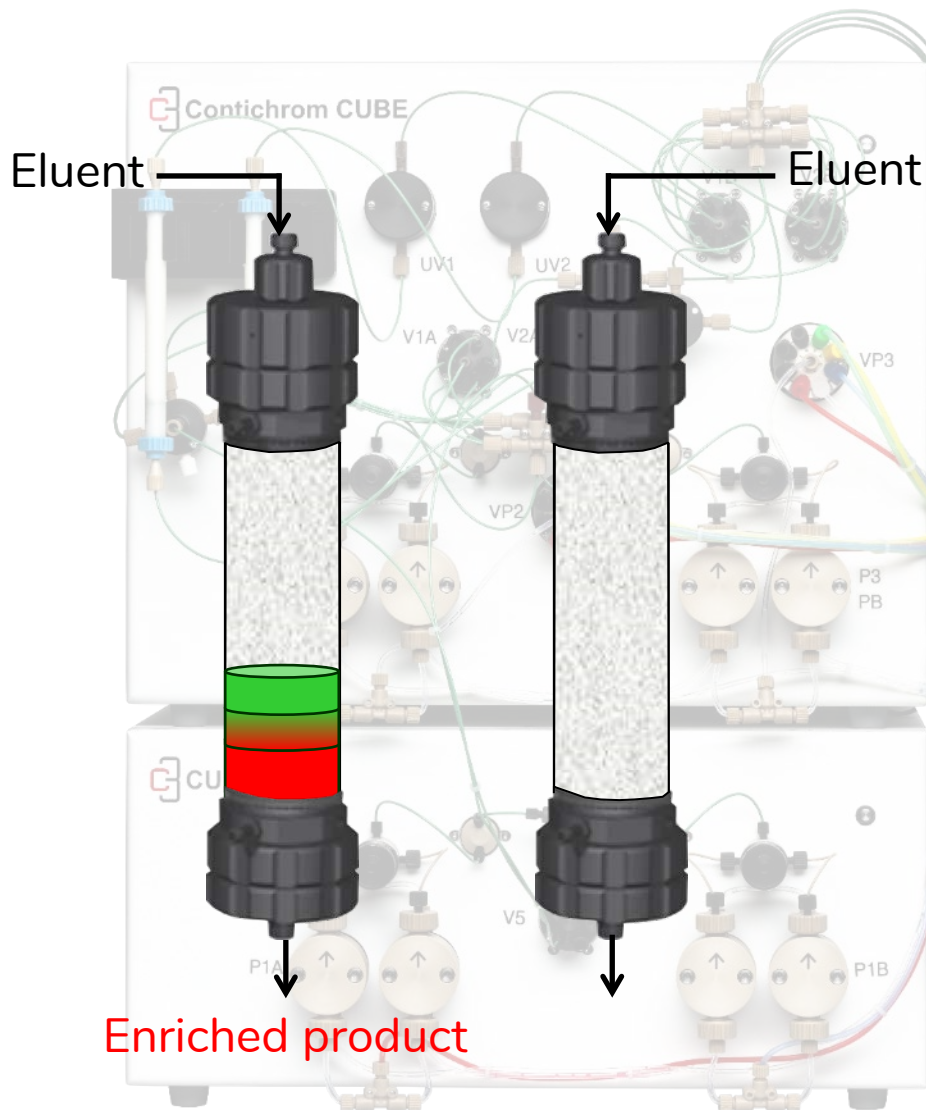
Step 4:

- recycle product

Start over



# Contichrom and N-Rich explained



## Step 1:

- feed column
- elute waste

## Step 2:

- recycle product

## Step 3:

- feed column
- elute waste

## Step 4:

- recycle product



Start over