

A Novel Chromatographic Technology: Enhancing Performance Utilizing a Modular Lattice Supported Resin Bed

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1. CHROMASSETTE® TECHNOLOGY*

A novel adsorptive device platform having...
 ... the separation capability of conventional chromatography,
 with the features and benefits of a cassette format
 ... distinguished by a supporting bed scaffold
 ... capable of accepting any bead
 ... protected by US patents and pending patent applications†

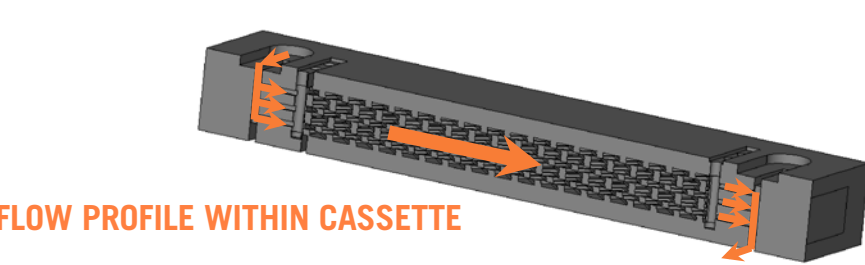
Proven technology in early development

*Technical Collaboration with SPF Technologies and JSR Life Sciences
 † Protected by US and foreign patents: US Patent 9120037, Foreign Patents, Other patents pending – Inventor Gastón de los Reyes

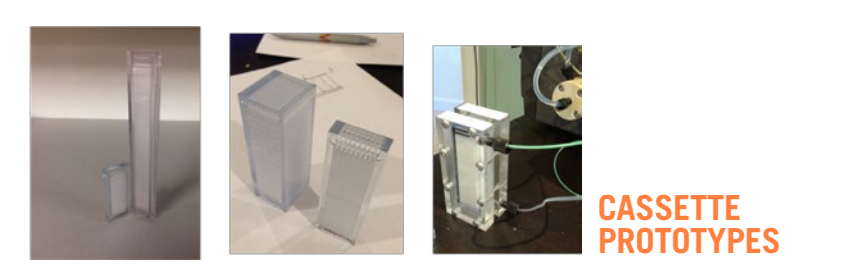
2. CHROMASSETTE TECHNOLOGY TARGETS

- 1. Modular Chromatography platform**
 - Pre-packed, reliable devices
 - Linearly scalable
 - Stackable → low hold-up volume
- 2. Intrinsic Bed Support**
 - Stable, robust bed even with soft compressible beads
 - Enables high velocity > 1000 cm/hr → Hyper-Productive® processes
 - Eliminates constraints imposed today by current chromatographic materials
- 3. Versatile Platform**
 - Any bead
 - Infinite configurable, many footprints possible
 - Rich in possibilities

3. CHROMASSETTE 3D PRINTED DEVICE



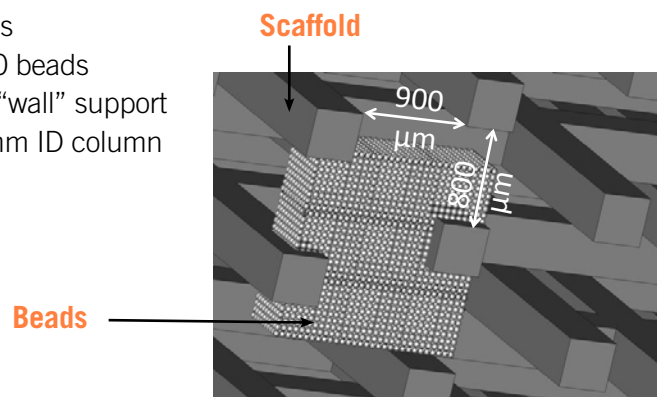
FLOW PROFILE WITHIN CASSETTE



CASSETTE PROTOTYPES

4. CHROMASSETTE SCAFFOLD

- Scaffold supports beads
- Distance to wall: 8 ~ 20 beads
- All beads benefit from "wall" support
- Equivalent to a 1 ~ 2 mm ID column



Scaffold
900 μm
1800 μm
400 μm

Beads

5. 100-L CONVENTIONAL COLUMN VS. 100-L CHROMASSETTE ASSEMBLY



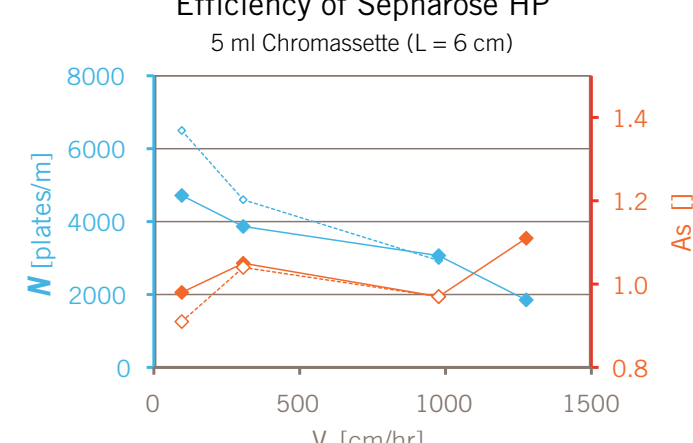
Easy to stack • Easy to store • Easy to configure • Universal Holder • Open Source

6. CHROMATOGRAPHIC PERFORMANCE OF CHROMASSETTE DEVICES

- Asymmetry, HETP, pressure drop
- Scaling and Parallel Operation
- Operation with compressible resins
- Performance in Bind & Elute Processes
- Productivity Gains: Chromasette Platform and Resin Design

7. BED STABILITY: AS AND HETP

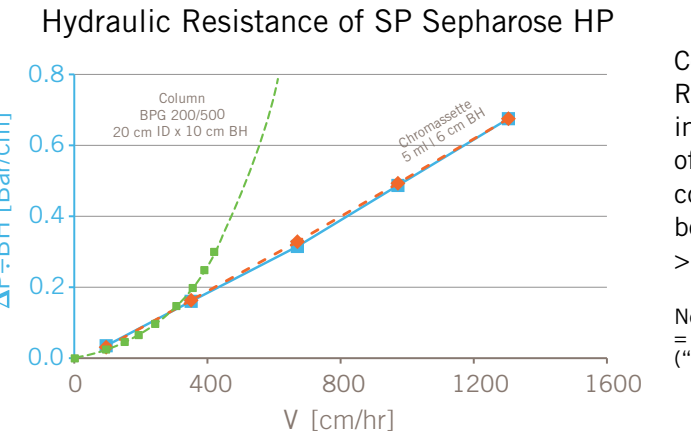
Efficiency of Sepharose HP
5 ml Chromasette (L = 6 cm)



Efficiency independent of flow direction even with compressible SOFT beads at > 1200 cm/hr

8. BED STABILITY: LINEAR PRESSURE DROP

Hydraulic Resistance of SP Sepharose HP

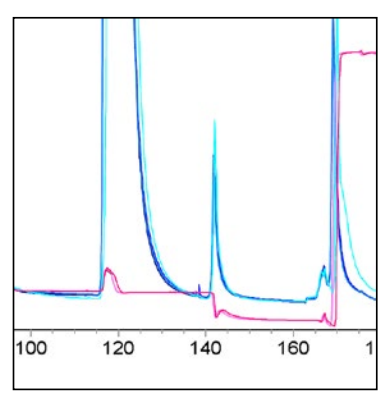


Constant Hydraulic Resistance independent of velocity with compressible SOFT beads at velocities > 1200 cm/hr

Notes: Vertical axis = Pressure Gradient ("Normalized ΔP")

9. CHROMATOGRAPHIC EFFICIENCY: BIND AND ELUTE MAB CAPTURE: COLUMN VS. CHROMASSETTE

Amsphere A3™ Overlay of 3 Chromasette + 1 column runs



- Equivalent Dispersion
- Indistinguishable from column

10. PRODUCTIVITY IN BIND & ELUTE PROCESSES INTEGRATION OF RESIN DESIGN AND CHROMASSETTE

- Where are the regions of higher productivity?
- How to exploit Chromasette supported bed?

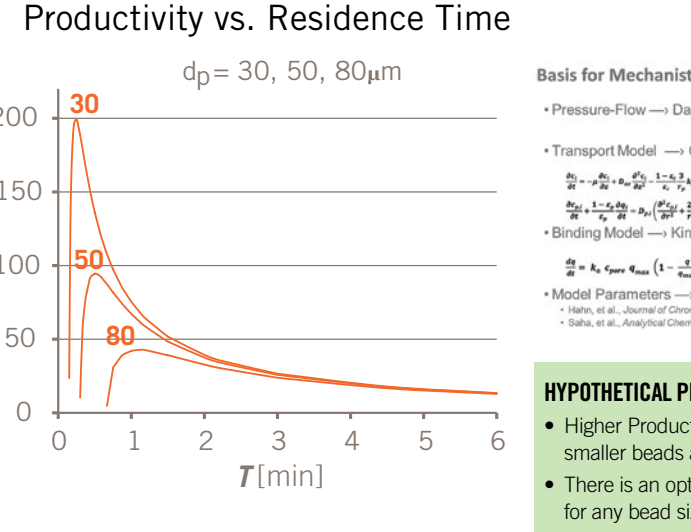
How to get there:

- Bead diameter – smaller gives higher DBC
- Pore size – larger leads to faster binding
- Multiple cycling – > 10 cycles per batch
- Higher pressure operation – if required

- **Productivities of 100 g/l/hr are achievable**
- The norm today is 10-20 g/l/hr

11. Productivity vs. Residence Time

$d_p = 30, 50, 80 \mu m$



Basis for Mechanistic Modeling

- Pressure-Flow → Darcy's Law $\Delta P = \frac{150 \mu L (1 - \epsilon)^2}{\epsilon^3} \frac{v}{k}$
- Transport Model → General Rate Model $\frac{\partial C}{\partial t} + v \frac{\partial C}{\partial z} = D \frac{\partial^2 C}{\partial z^2} + \frac{1}{\tau} (C - C_{in})$ Axial dispersion in Column
- Binding Model → Kinetic Langmuir $\frac{\partial C_b}{\partial t} + v \frac{\partial C_b}{\partial z} = k_a C (C_{max} - C_b) - k_d C_b$ Diffusional Resistance in Beads
- Model Parameters → Literature for MabSelect™ Resin $\frac{\partial C_b}{\partial t} + v \frac{\partial C_b}{\partial z} = k_a C (C_{max} - C_b) - k_d C_b$ Mab Adsorption/Desorption

HYPOTHETICAL PRODUCTIVITY ANALYSIS:

- Higher Productivity possible with smaller beads and bigger pores
- There is an optimal residence time for any bead size

12. EVALUATION OF AMSPHERE ProA VARIANTS: PRODUCTIVITY PROOF OF PRINCIPLE

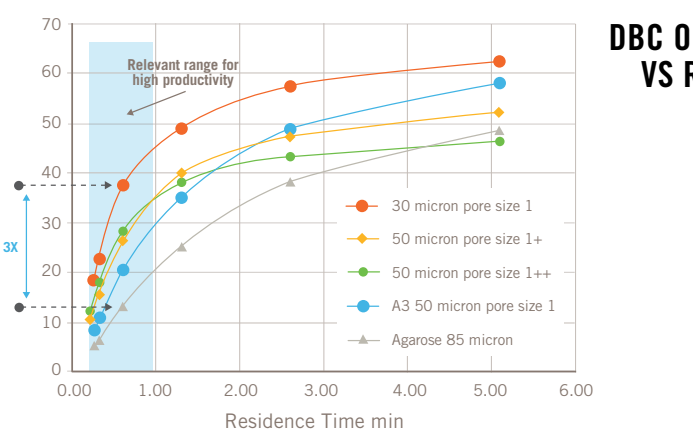
Protein A variants;

- Same base beads same chemistry and same ligand

- A3 - standard 50 micron product
- 50 micron with larger + pore size
- 50 micron with larger ++ pore size
- 30 micron prototype with standard pore size
- Agarose S for comparison 85 micron

13. ProA VARIANTS

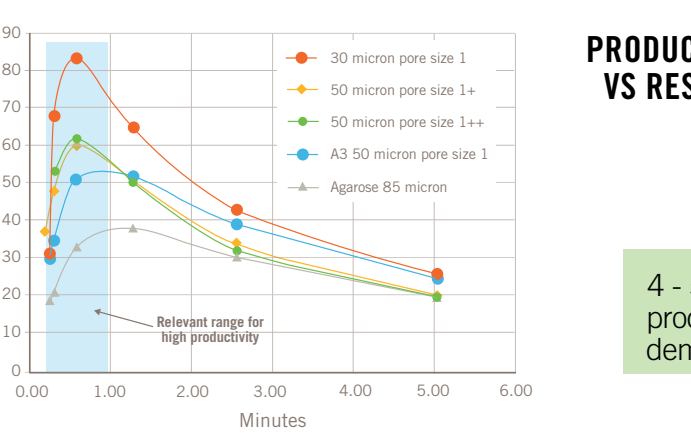
DBC OF POLYCLONAL IgG VS RESIDENCE TIME @10% BT



- 30 micron pore size 1
- 50 micron pore size 1+
- 50 micron pore size 1++
- A3 50 micron pore size 1
- Agarose 85 micron

14. PRODUCTIVITY OF ProA VARIANTS

PRODUCTIVITY (g/l/hr) VS RESIDENCE TIME (MINS)



- 30 micron pore size 1
- 50 micron pore size 1+
- 50 micron pore size 1++
- A3 50 micron pore size 1
- Agarose 85 micron

4 - 5x higher productivity demonstrated

SUMMARY

1. First practical modular chromatography platform
2. Chromasette supported-bed enables packing of any resin bead
3. Constant bed permeability, independent of resin compressibility at > 1500 cm/hr
4. Truly linear scalable
5. Eliminates packing methods and equipment
6. New operating domains and resin design are now possible for both bind & elute and flow-through
7. Hyper-Productive® process may enable single use chromatography

Stay tuned for on going developments