BIA separations
Leaders in Monolith Chromatography

BIA Separations

CIMmultus™ Monoliths – tailored to accelerate process development and address large scale manufacturing of ATMPs and Vaccines.

Ingo S. Nagler, BDO

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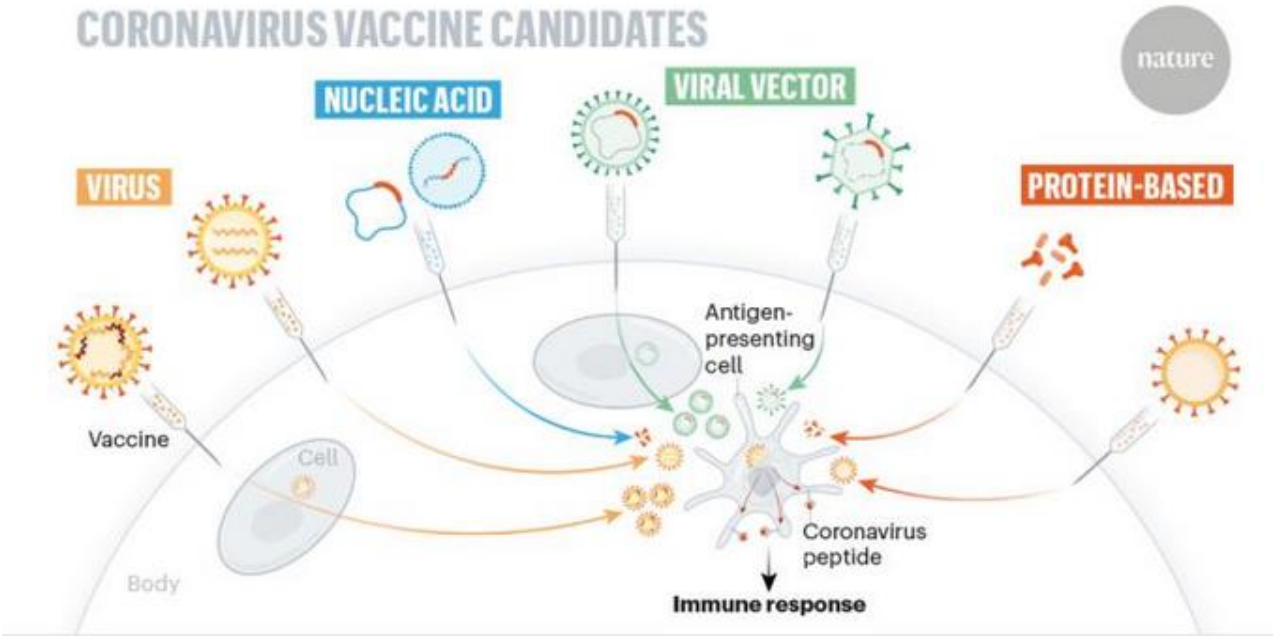
CIMmultus™ Monoliths

A versatile technology platform covering all large , complex vaccine canditates



Source:
The race for coronavirus vaccines: a graphical guide.
Nature **580**, 576-577 (2020)

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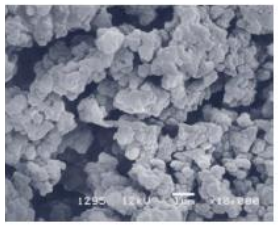
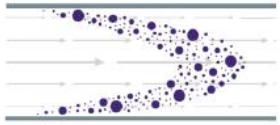
CIMmultus™ Monoliths

Inherent design properties facilitate yield, productivity and potency

Inherent design properties of BIA's monolith technology...



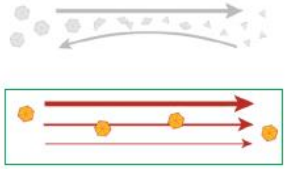
Continuous structure (sponge-like)
- Consistent channel diameter throughout the entire bed
- Channel volume is about 60% of total monolith volume
- Creates high flows with minimal pressure drop



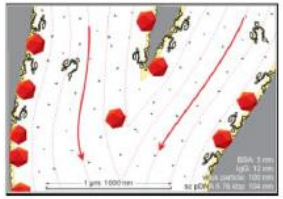
Convective mass transport; laminar flow
- Capacity and quality of fractionation are independent of flow rate and size of molecule
- Flow runs parallel to its channel walls, precluding eddy formation

Highly interconnected channels
- Laminar flow in monoliths limits solute dispersion to laminar dispersion and dispersion caused by partially lagging solutes of the solute front
- Without irregular cavities, laminar flow is maintained through branching flow paths

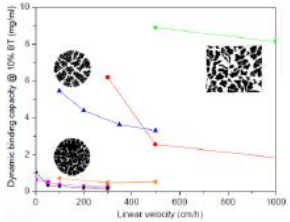
...Reduce shear stress, increase yield, and increase productivity



Low shear stress and dispersion; higher resolution
- Absence of a void volume avoids dispersion and shear, two consequences of incumbent methods, leading to higher resolutions and eluted product concentration
- Leads to exponential increases in yield rates by up to 80%



Better productivity
- Continuous and uniform flow throughout the column bed results in greater volumes, faster speeds, and lower pressures within the column
- Monolith technologies results in lower manufacturing costs by as much as 3x when compared to traditional particle (diffusion) columns



Highest binding capacity
- Binding and elution occur at channel surfaces, supporting instantaneous transfer kinetics, contribution to efficient surface utilization (e.g. high binding capacity)
- 10x product yield compared to incumbent methods and a proportional reduction in material costs, production area space, hardware size, etc.

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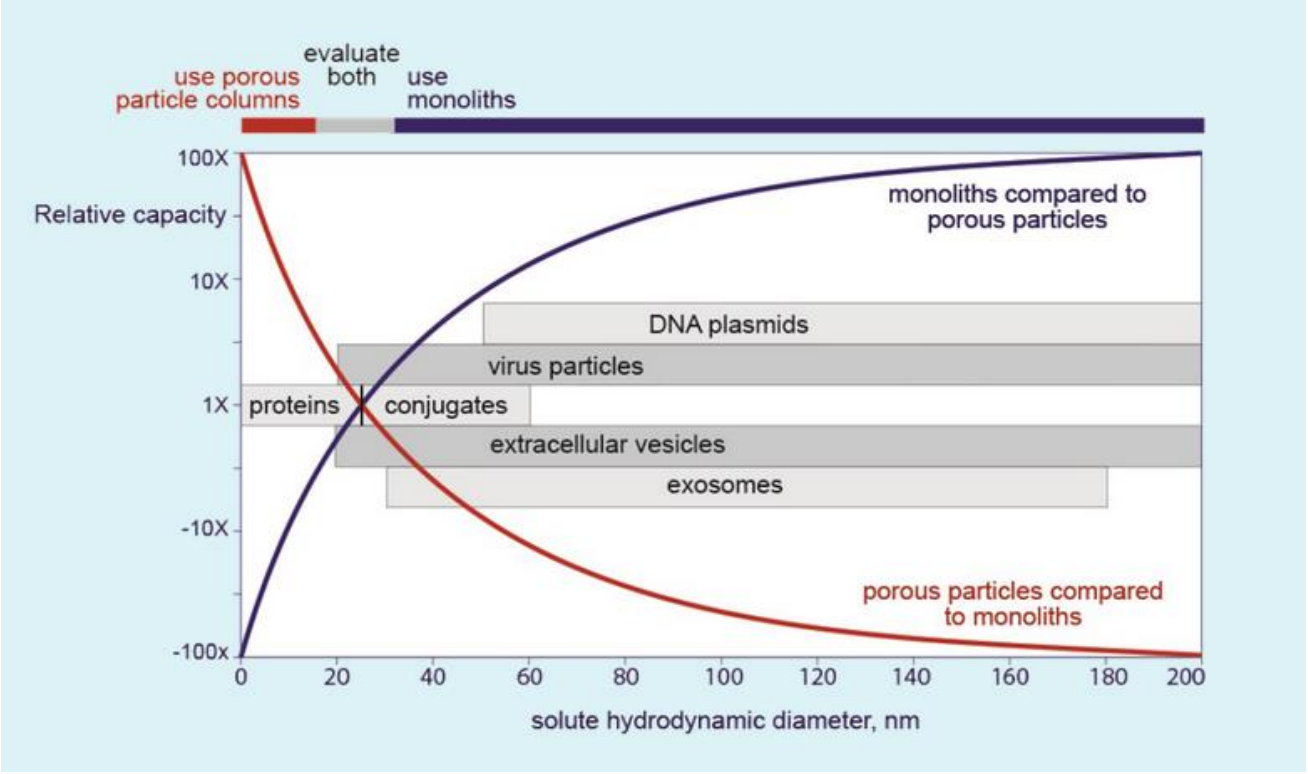
Chromatography of large, complex biomolecules by design



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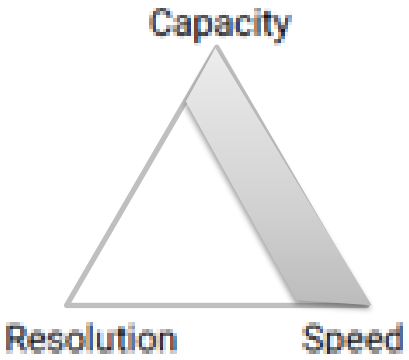
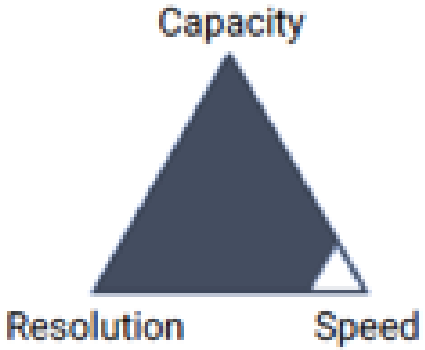
CIMmultus™ Monoliths

Monoliths outperform conventional media in **large biomolecule** chromatography applications due to inherent design properties.

Membranes

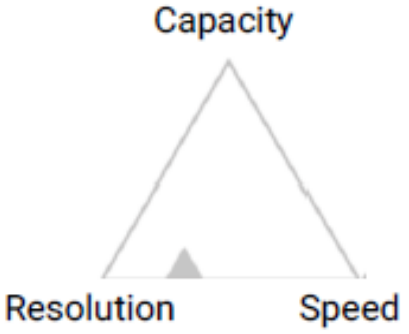


Monoliths



Flow independant capacity
Flow independant resolution

Porous Particles



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CIMmultus™ Monoliths

Monoliths have contributed to 100`s of clinical batches of pDNA, including market supply.

40L

CIMmultus™.

Pre-packed.

Multi-Use.

200g

Plasmid DNA

Ultra Pure.

Per cycle.

- COVID pDNA vaccine dosing estimated in low mg range
- HIP(2) Process Pack generic protocoll
- Extreme productivity needed
- No compromise in purity
- Analytical technology in place

https://www.businesswireindia.com/plasmid-dna-manufacturing-technology-co-developed-by-boehringer-ingelheim-austria-with-bia-separations-6924.html

https://www.lisavienna.at/news/biomay-and-bia-separations-collaborate-on-production-and-purification-of-large-dna-plasmids/

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CIMmultus™ Monoliths

Monolith based mRNA purification portfolio solves capturing and polishing problem at manufacturing scale

8L

CIMmultus™.

Pre-packed.

Single or Multi-Use.

16g

mRNA

Ultra Pure.

Per cycle.

- COVID mRNA vaccines dosing estimated in 5-200 ug range
- Broad Portfolio of 5 chemistries
- dsRNA impurity removal solved
- No compromise in purity
- Analytical technologies in place

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CIMmultus™ Monoliths

Monolith based VLP purification outperforms productivity of density gradient centrifugation based method by factor 200*

8L

CIMmultus™.

Pre-packed.

Single or Multi-Use.

E19

Virus Like Particles

Ultra Pure.

Per cycle.

- COVID VLP vaccine dosing estimated in E9-E11 range
- Capturing and polishing chemistries in place
- Critical Chromatin impurity removal technology in place
- Analytical technologies in place

- https://www.sciencedirect.com/science/article/pii/S0021967316306446

BIA separations
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CIMmultus™ Monoliths

Monolith based AAV *purification follows capturing and polishing strategies of Gene Therapy vectors – BIA has large scale market supply experience**

8L

CIMmultus™.

Pre-packed.

Single or Multi-Use.

E17$_{vg}$

AAV Vector

Ultra Pure.

Per cycle.

- Capturing and polishing chemistries in place
- Critical Chromatin impurity removal technology in place
- Market leading empty/full separation in place
- Analytical technologies in place

*: https://www.nytimes.com/2020/05/04/health/gene-therapy-harvard-coronavirus.html

**: https://bioprocessintl.com/bioprocess-insider/upstream-downstream-processing/bia-separations-providing-chromatography-columns-for-avexis/

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CIMmultus™ Monoliths

Example of Live Influenza (Flu) Process Intensification

8L

CIMmultus™.

Pre-packed.

Single or Multi-Use.

2.4E14 FFU*

Influenza serotype

Clinical Quality.

Per cycle.

Clarified benzonase treated Vero cell harvest

↓

Chromatography using CIMmultus™ SO3

↓

Formulation/sterile filtration

* Capacity is very much depending on the impurity profile of the feedstock. For pure Influenza Virus the capacity would be in the range of E15.

M. *Tajnik* Sbaizero, M. Wolschek, M. Reiter, T. Muster, P. Gagnon, A. Štrancar
https://bioprocessintl.com/downstream-processing/chromatography/intensification-of-influenza-virus-purification-from-clarified-harvest-to-formulated-product-in-a-single-shift/

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CIMmultus™ Monoliths

Example of Live Influenza (Flu) Process Intensification

Thank you very much for your attention!
For all further questions, please contact:
ingo.nagler@biaseparations.com

Left buliding: current facility
Right building: under construction
Total: 7000 m2