



Life Sciences



## **Mixed Mode Chromatography**

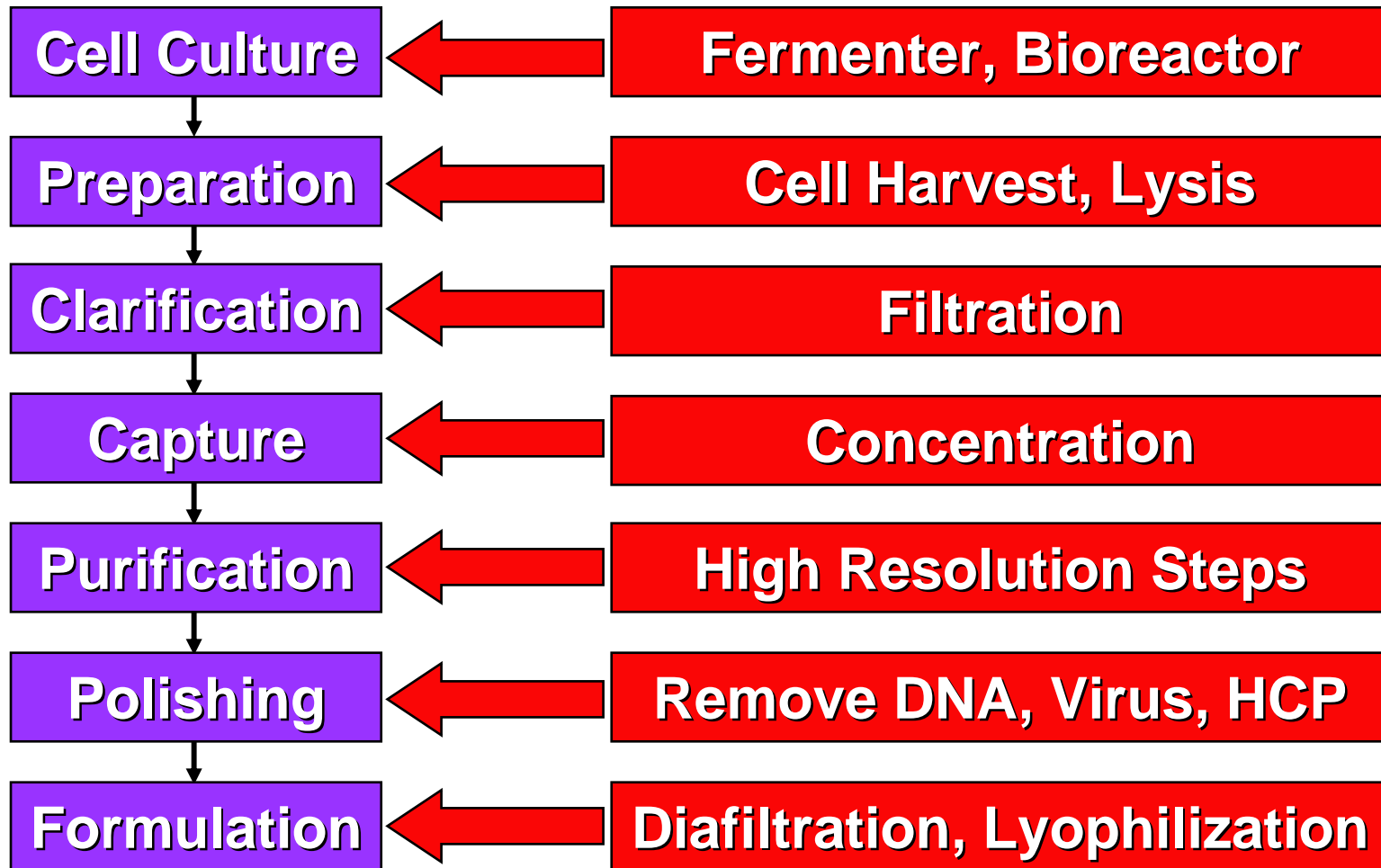
**A multimodal separation technique for  
biopharmaceutical purification**

Peter R. Levison,  
Pall Life Sciences, Portsmouth, UK

**SCI, London, 27<sup>th</sup> June 2007**



## Biologicals Manufacture





## Biologicals Manufacture

- Train of discrete orthogonal process unit operations
- Sequential
- Typically carried out in separate process areas, but within a single closed facility
- Highly regulated

## Biologicals Manufacture

- Process economics and process intensification are key drivers for change
- Manufacturing strategies of the future will be driven by integrated unit operations that:
  - Minimise down-time
  - Maximise throughput
  - Optimise cost
  - **Enhance productivity**





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# Orthogonal Chromatographic Processes for Biologicals Manufacture

## Adsorptive

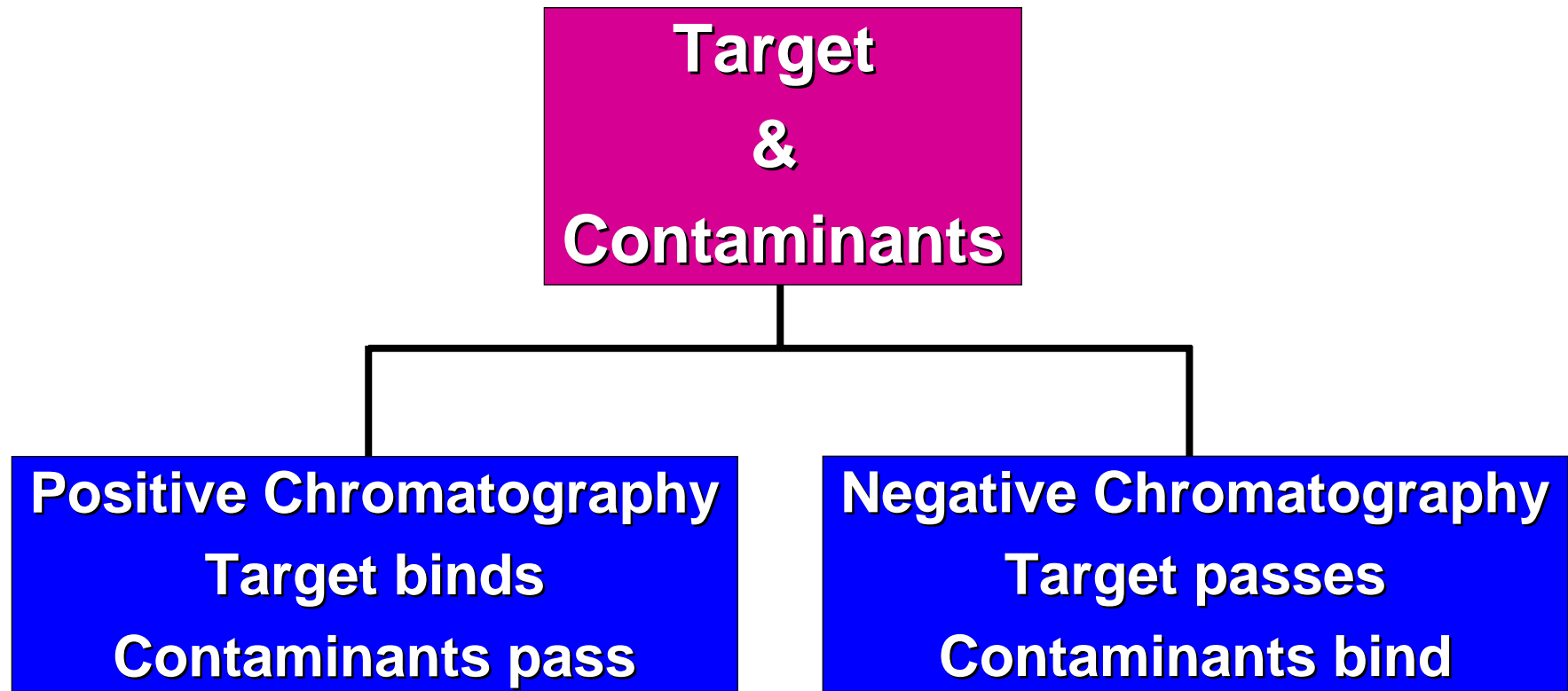
- Ion-exchange
- Hydrophobic
- Affinity
- Chelating
- Thiophilic
  
- Hydrophobic charge induction
- Mixed mode

## Partitioning/Sieving

- Normal phase
- Reversed phase
- Size-exclusion



## Adsorption Chromatography





## Adsorption Chromatography

### Negative Chromatography:

- Effects purification
- No concentration
- Constant mobile phase
- Shortest process time
- Regeneration & elution can be one operation
- Simplest validation

### Positive Chromatography:

- Varying mobile phase
- Longer process time
- Concentrates target
- Regeneration follows elution
- Effects purification
  - Additional reagent costs
- Complex validation



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## Process-Scale Chromatography

### Stages of a Purification:

**Capture**

**Purification**

**Polishing**

**Mixed  
Mode**



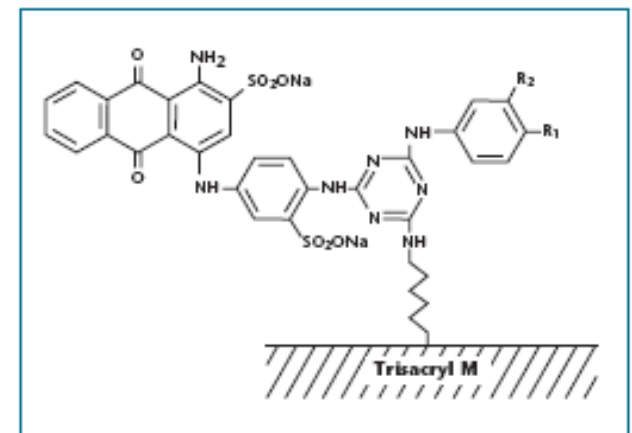


## Mixed-Mode Chromatography

- Exploitation of multiple, distinct protein-ligand interactions to adsorb target proteins or impurities.
- Offer new solutions to separations where traditional chromatographic methods are not effective.
  - Where feedstream conductivity is too high for efficient capture on traditional ion exchange resins.
  - Purifications by Hydrophobic Interaction (HIC) that would require massive addition of lyotropic salt.
  - Separations where affinity ligands are not cost effective.
- **Is it new??**

## Mixed-Mode Chromatography

- Affinity interactions exploit multi-site attachment of the ligand to topological features of the adsorbate by various chemical interactions.
- **This is mixed mode!!**
- Cibachrom blue is a well established ligand in plasma fractionation for albumin removal
- **This is mixed mode!!**





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## Mixed Mode Chromatography Conference

- Series of presentations on mixed mode chromatographic media from the leading vendors supplying the industry
- Applications of mixed mode chromatography by leading academic and industrial groups
- Opportunity for networking and discussion throughout the day.
- **Welcome**