

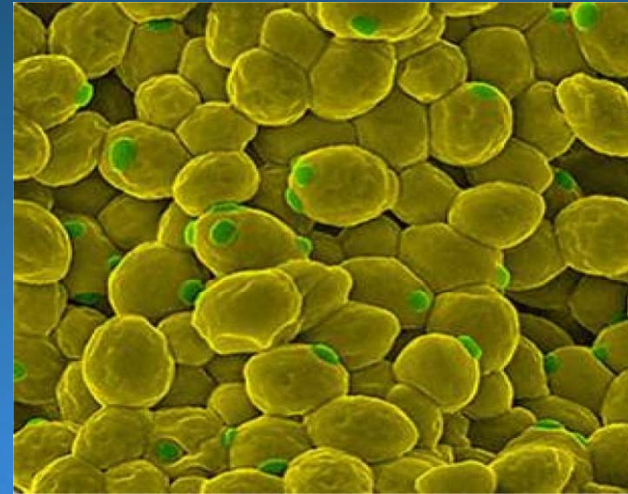


CELL DISRUPTION BY HIGH- INTENSITY ULTRASOUND - A POTENTIAL INDUSTRIAL- SCALE TECHNIQUE

Cell Disruption

- **Many biologically interesting molecules are produced by culturing in bacterial or yeast cells**

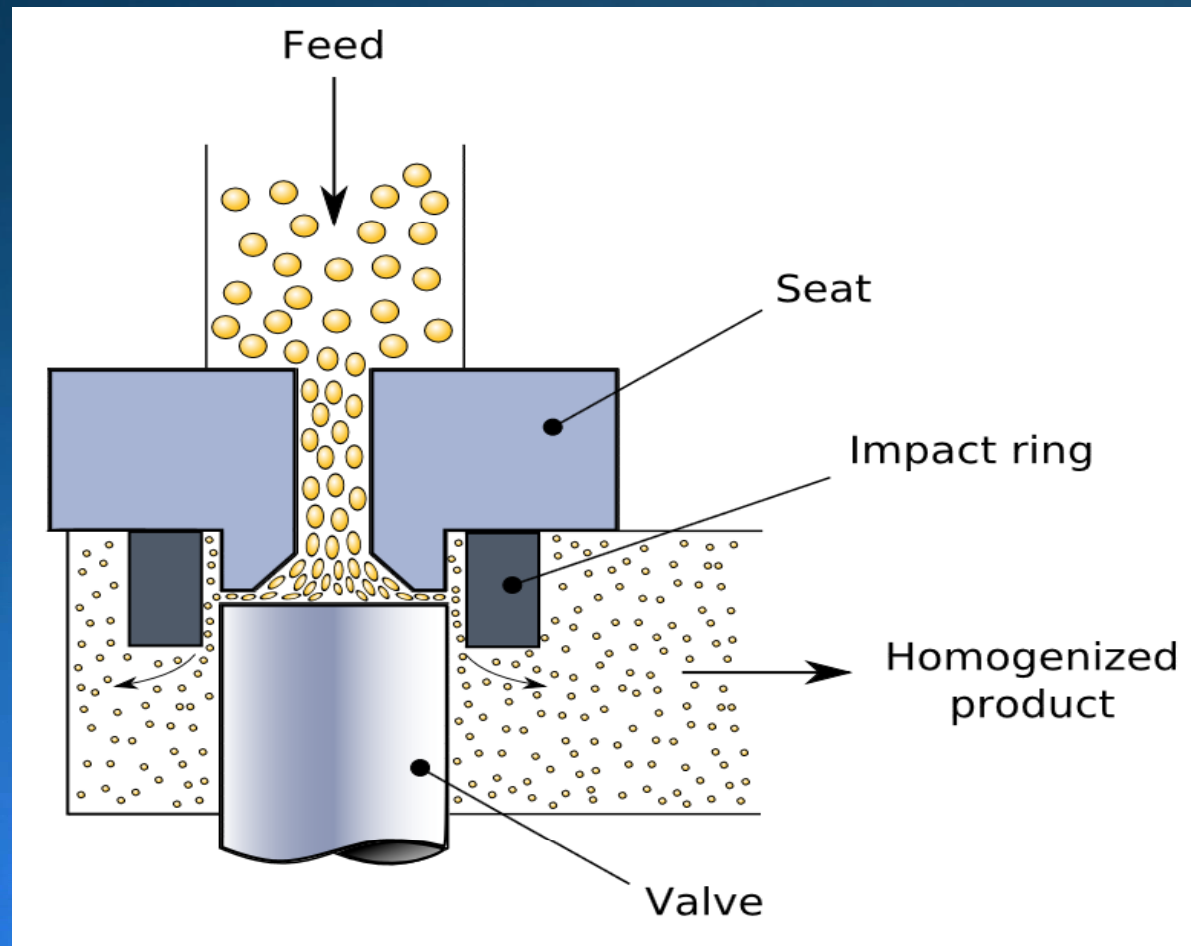
- Antibodies
- Enzymes
- Hormones
- Cytokines
- Clotting factors
- Vaccines



- **Cell disruption (lysis) is a method for releasing biological molecules from inside a cell**
- **Global sales for biopharmaceutical proteins ~ \$170 Billion**

Current Industrial Technologies

High Pressure Homogenization (HPH)



High Pressure Homogenization (HPH)

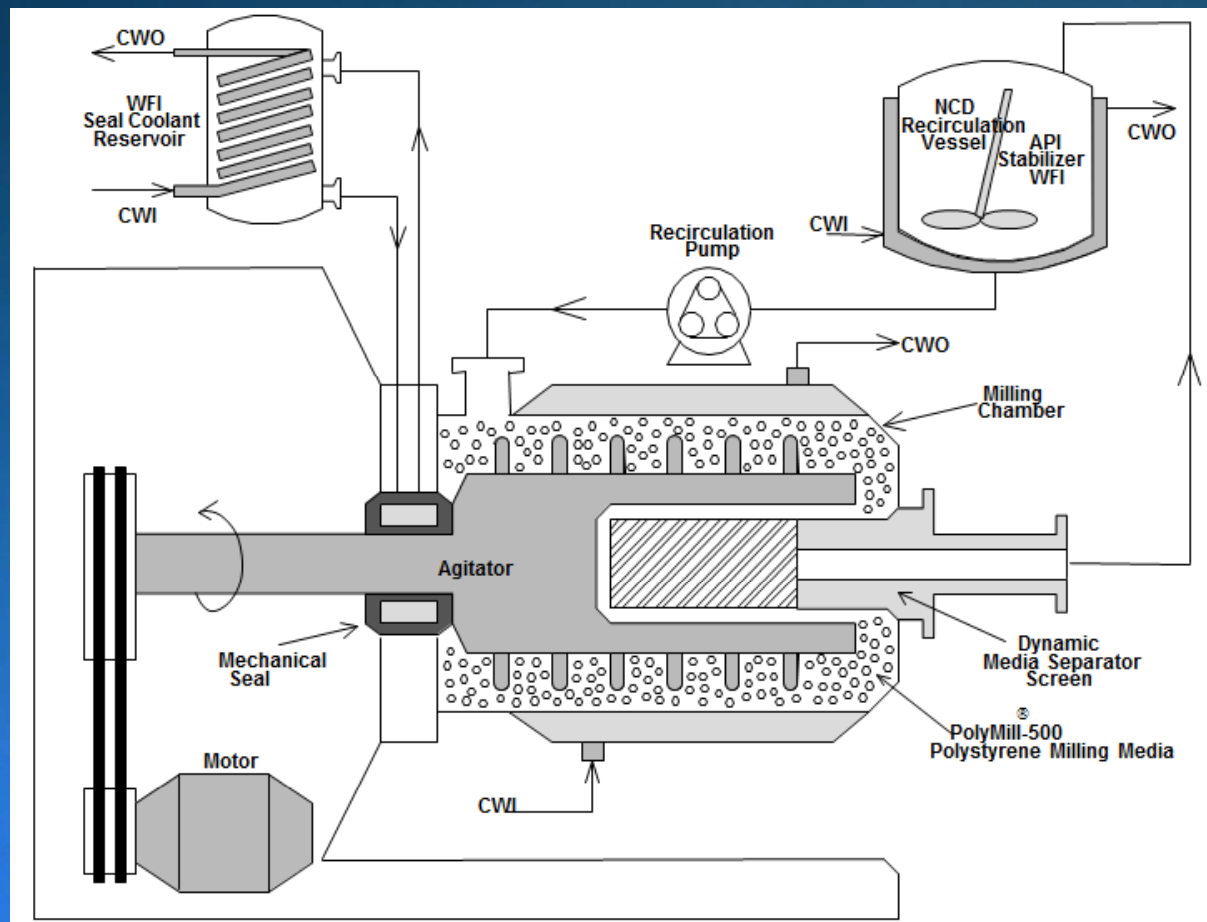
- Currently the main method (90% of the market)
- Used for bacteria and yeast disruption

Drawbacks:

- Pre-processing by non-mechanical techniques
- Heating
- Consumes a lot of energy, damageable valves, expensive maintenance

Current Industrial Technologies

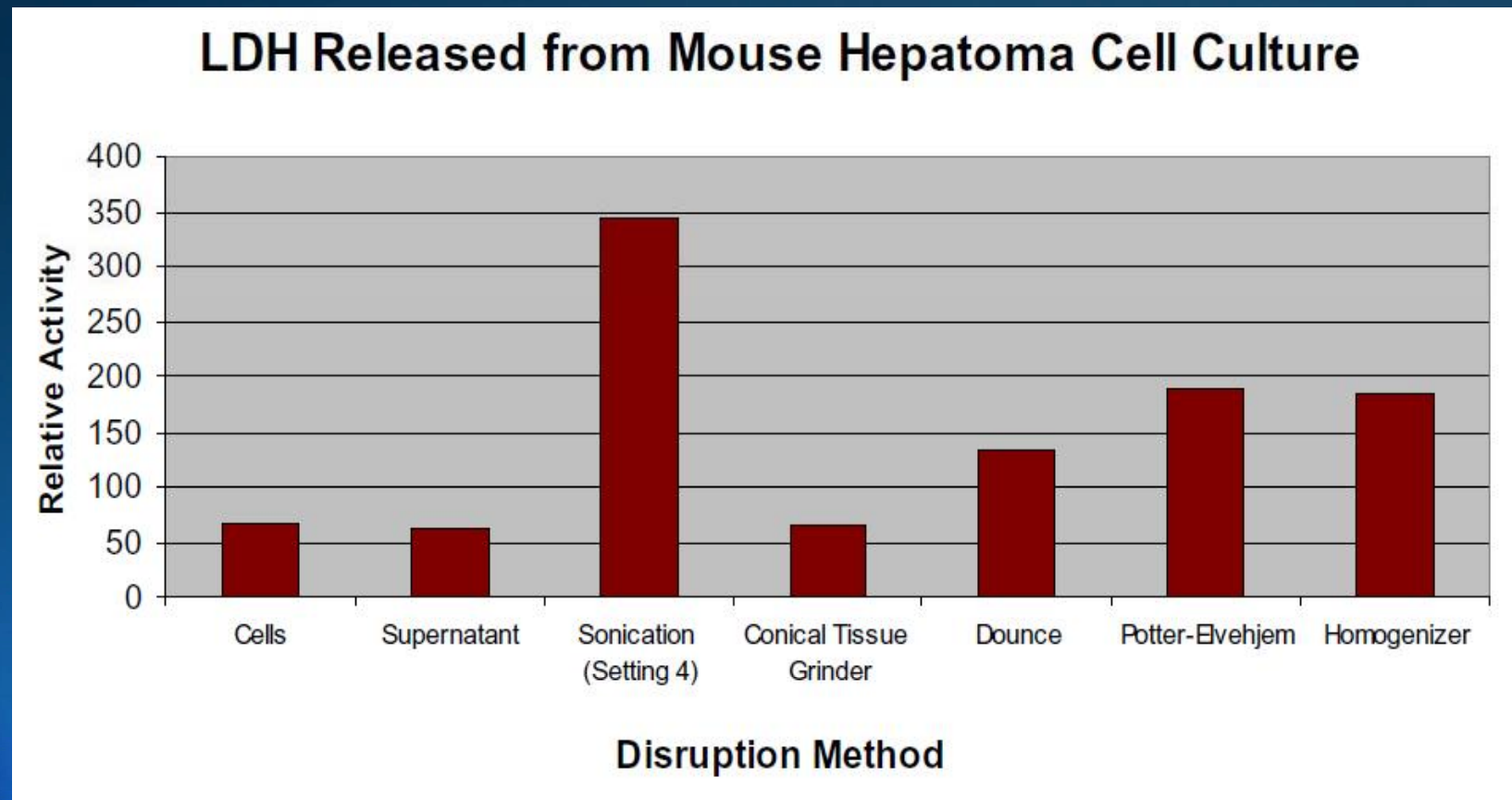
Wet Media Milling (WMM)



Wet Media Milling

- Mills are less popular within pharmaceutical industry (<10% of the market)
- Media occupies 80-90% of the packed volume
- Frequently used in combination with chemical disruptors
- Drawbacks: significant protein denaturation because of high temperature and/or excessive shear, wear of the grinding media

Sonication vs. Other Methods



- **Ultrasonic cell disruption is a laboratory standard**

Burden, D. W. Guide to the Homogenization of Biological samples. *Random Primers*, 2008. 7:1-14.

Sonication vs. Other Methods

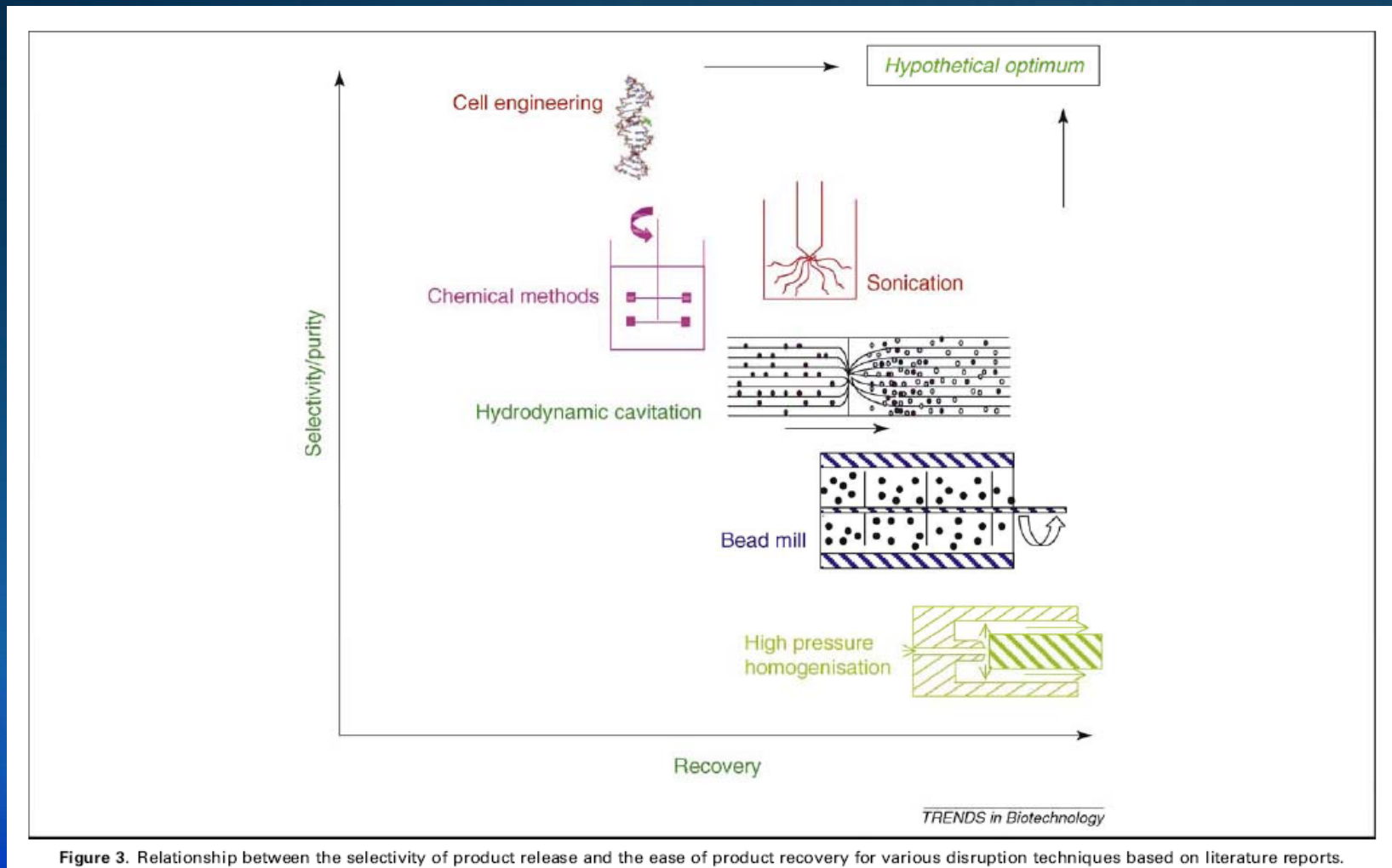


Figure 3. Relationship between the selectivity of product release and the ease of product recovery for various disruption techniques based on literature reports.

Balasundaram, B., S. Harrison, et al. (2009). *Trends Biotechnol* 27(8): 477-85.

Conventional Ultrasonic Technology

Ultrasonic Cell Disruption – **HIGH AMPLITUDES** ARE
REQUIRED



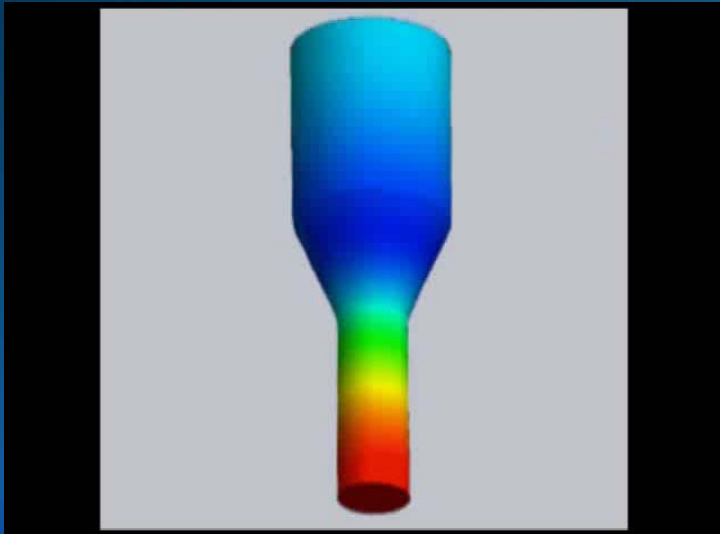
- High-Quality Product
- Low-Cost Equipment
- Simple Aseptic Processing
- Selective Extraction



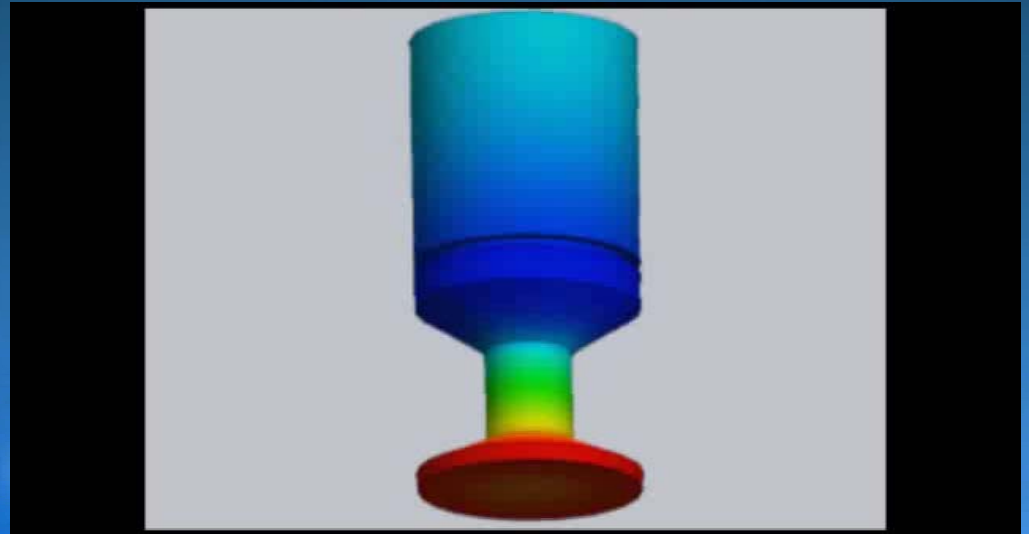
Barbell Horn Ultrasonic Technology

- Scale up without lowering the amplitudes

CH



HBH

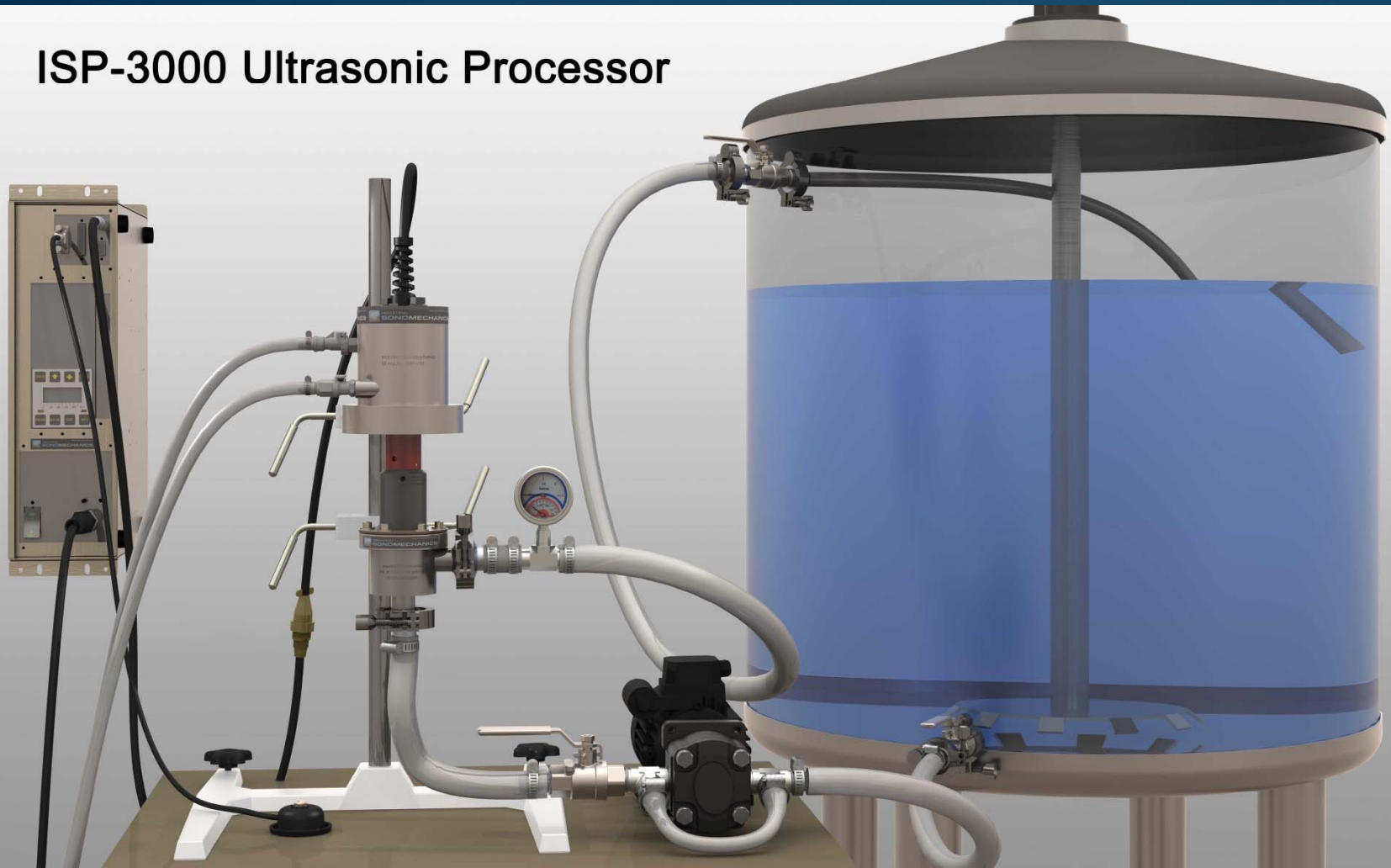


$$\text{Scale-up Factor} = 2(D_{\text{hbh}}/D_{\text{ch}})^2 \approx 25 - 50$$



Barbell Horn Ultrasonic Technology

ISP-3000 Ultrasonic Processor



Ultrasonic Disruption of *S. cerevisiae*

Laboratory scale – LSP-500

Bench scale – BSP-1200

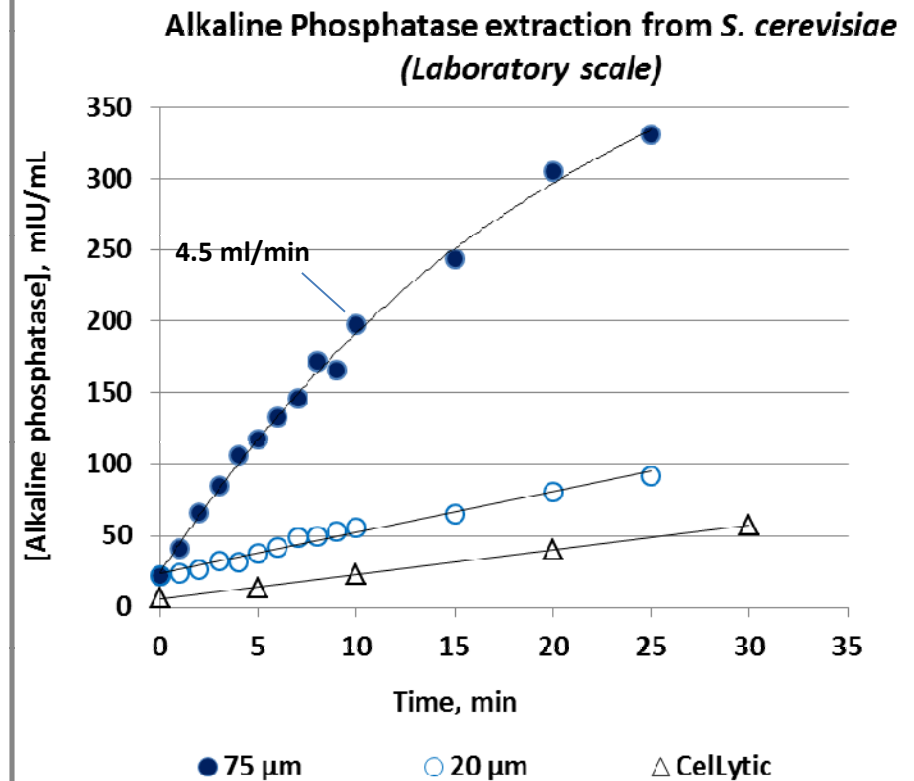
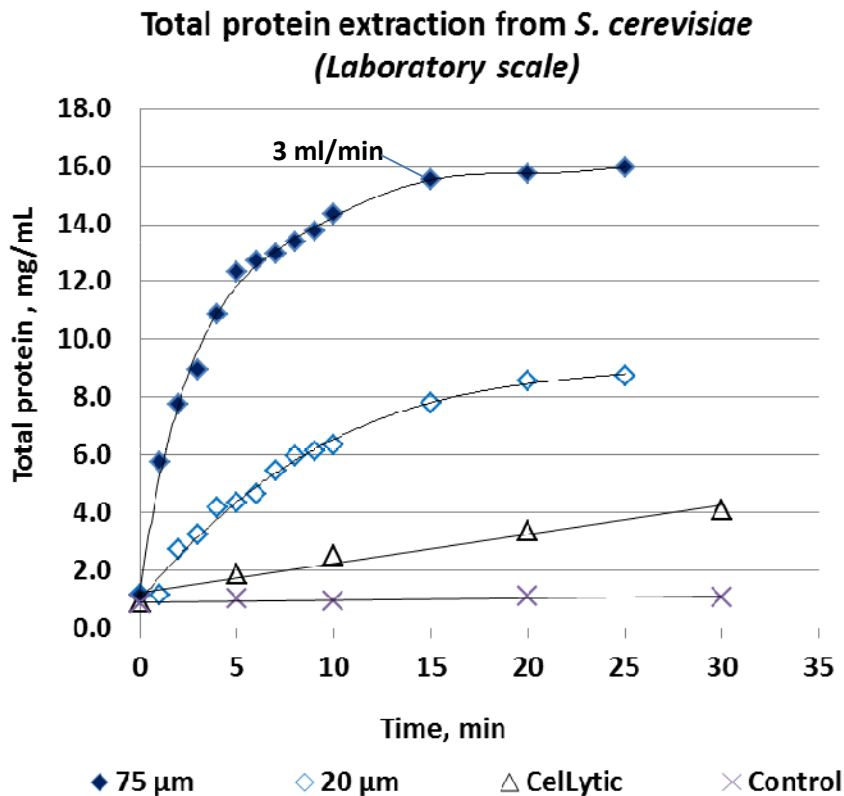


CH-type horn, $\varnothing = 12.7$ mm



HBH-type horn, $\varnothing = 32$ mm

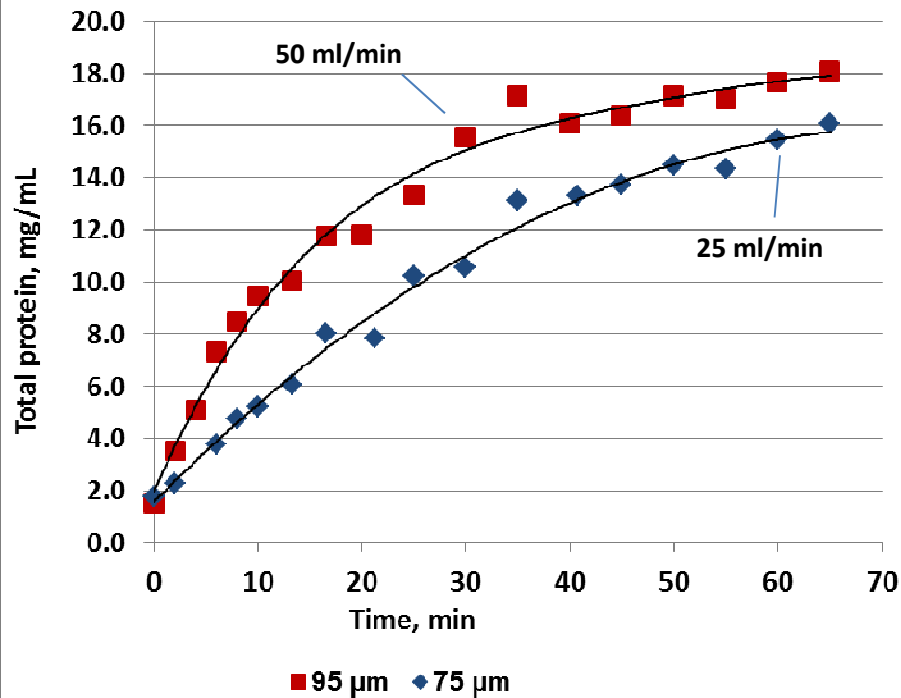
Sonication Versus Chemical Extraction, Laboratory Scale (45 ml)



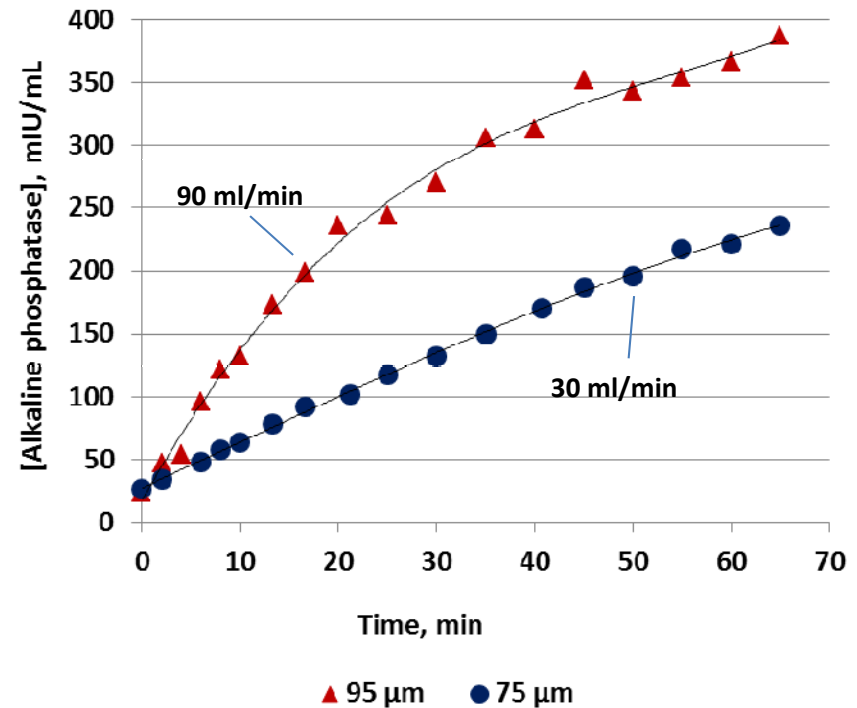
Ultrasonic amplitude is important!

Sonication with BHUT, Bench Scale (1500 ml)

**Total protein extraction from *S. cerevisiae*
(BHUT, Pilot scale)**



**Alkaline Phosphatase extraction from *S. cerevisiae*
(BHUT, Pilot scale)**



Ultrasonic amplitude is important!

CONCLUSIONS

- **BHUT – effective for cell disruption**
- **High amplitudes are essential**
- **Directly scalable**

- **Proven laboratory standard method can now be taken to the production scale**



INDUSTRIAL
SONOMECHANICS

www.sonomechanics.com



**Allied Innovative
Systems**

THANK YOU

Q&A