

# Painless Particles<sup>®</sup>

Quarterly Global Newsletter  
Volume 13, #4, December, 2000



Now including Flow Cytometry Standards Corp.

**B E A D S • A B O V E T H E R E S T<sup>™</sup>**

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## ISO-9002 Certification



BLI has been certified by TRA Certification as having a Registered Quality System—ISO 9002.

## Bargain

### "Bangs ^ Beads"— on the web

Check this on-line list for special prices on small quantities of end-of-run, "close-outs," or left-over lots of our regular microspheres— all sizes, surface chemistries, and colors, plus *ProActive<sup>®</sup>*. They're ideal for folks just starting "bead work."

**OverFlow<sup>™</sup> Beads:** See the FCSC surplus beads list (at [www.fcstd.com](http://www.fcstd.com)) for odd lots and non-stock items. These 1-8  $\mu\text{m}$  diameter fluorescent-dyed beads were made for flow cytometry, but may be interesting for other applications.

These lists are up-dated at least monthly, so check back regularly for special deals.

## QuantumPlex<sup>™</sup> – a Crossover Product <sup>NEW</sup>

*Say what?* OK, let's examine this carefully. We used "Quantum" to capitalize on the **Quantum<sup>™</sup>** trademark from FCSC since these *are* fluorescent dyed beads— but for a different application. The "**plex**" refers to multiplex assays. We designed them, at customer request, for situations where you want to assay for several different analytes simultaneously. We call this a "crossover product" because it really does blend, merge, and bridge the two parts of our business (beads for assays and flow cytometry beads) for the first time. We used our proprietary dyeing technology and our **ProActive<sup>®</sup>** coating technology to make these complex beads.

*So, what is it?* QuantumPlex is an innovative new kit for multiple analyte detection research applications in flow cytometry. A breakthrough for screening assays, **QuantumPlex** allows for detection of up to 20 different analytes per sample or efficient screening of multiple samples. *The result?* Flexible, efficient, and cost-effective high-throughput research.

QuantumPlex kits consist of 5- or 10-bead sets of two uniform bead sizes, dyed with varying amounts of BLI's **Starfire Red<sup>™</sup>** dye, which are suitable for use with any flow cytometer. Goat anti-mouse IgG coating permits conjugation of mouse monoclonal antibodies to each bead to detect up to 20 analytes per sample.

So, if you have a flow cytometer or expect to get one soon, and if you want to do multiple assays on your flow instrument, then call us or write. Tell us what you want to do and we'll tell you how to use **QuantumPlex** to do your job. We'll send you more detailed information or you can check our website at [www.quantumplex.com](http://www.quantumplex.com) or either of our other web addresses ([www.bangslabs.com](http://www.bangslabs.com) or [www.fcstd.com](http://www.fcstd.com)) **QuantumPlex— maximizing flow cytometry!**

*What are you waiting for— some real data?* OK, we started with some standard polymer beads and dyed them with 4 different levels or intensities of dye. Our proprietary fluorochrome is excitable by either Ar or He/Ne laser with sharp emission in FL3 (and minimal carryover into FL1 or FL2). Then we coated the dyed beads with our special goat anti-mouse antibodies.

*Still with me? You must be somewhat interested.* Then we tested the beads in our flow cytometer (BD FACScan) and found that we indeed had a set of five beads. The set consists of a blank plus four narrow and cleanly separated peaks (NO overlap)— corresponding to the four different levels of fluorescence. Then we demonstrated that all the beads would collect mAb-FITC complex.

*But will they work outside BLI's lab?* We asked customers to do beta-site testing and they loved them (= bought them). So now it's up to you. What could *you* do with a **QuantumPlex** kit?

While we were waiting for customer response (yours and others), we decided to make another set of beads— a larger size, so that the set can be expanded to 10 beads (2 different diameters, each size with 4 different dye levels plus a blank for 5 beads per set).

Ultimately, we await your questions, your order, and your feedback as to how you like the **QuantumPlex** beads.

Did I mention that you can buy them here? Well, you can. Just ask for the following catalog numbers: #205 (Size 1/ IgG), #208 (Size 2/ IgG), or #209 (both sizes/ IgG) and we'll send you a set of 5 (or 10) bottles of 1, 5, or 10 ml (your choice) with 1.0 million beads per ml.

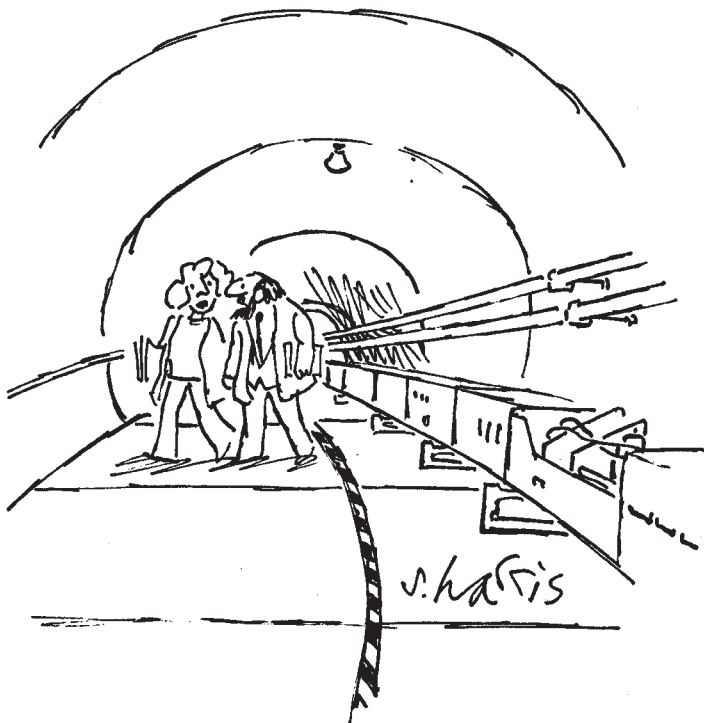
In the future, we'll also have #215 (Size 1/ Streptavidin), #218 (Size 2/ Streptavidin), and #219 (both sizes/ Streptavidin). What else is on your wish list?

## The Latex Course™ 2001 in CA

It's set for April 30-32; I mean, May 0-2; OK, it's *really* going to be **April 30–May 2, 2001**, in San Diego, CA. This will be our 14th version of this approximately annual, popular course wherein we tell all we know about making and using latex particles, microspheres, and polymer beads for diagnostic, flow cytometric, molecular biological, and other assay technologies.

As in the past, we are assembling about 8-10 respected international experts in this important field to share their collected wisdom for three days of lectures and discussion. All attendees get a course book to take home with copies of all lectures and slides for future reference, so you can sit back and absorb. Bring your questions and problems and we'll try to answer all.

The course brochure will be developed by year-end— as soon as we nail down all the speakers. I can tell you now that all the most popular speakers from past years have already agreed to repeat this coming spring in sunny California. Details will be in the brochure which we will send to you, and as soon as it is published, we'll have it up on our website. Look for it after the New Year starts. Registration starts – *now!*



"WHAT IF WE SPEND ALL THESE BILLIONS, AND THERE JUST AREN'T ANY MORE PARTICLES TO FIND?"



## The Latex Course 2000

Last Call for Book, "Diagnostic Applications of Latex Technology: Theory and Practice"

Until the books are gone or January 31, 2001, you can order extra copies of the course book (\$350 plus shipping for >500 pages of microsphere wisdom). For details, see May, 2000 brochure online. Order by phone, fax, or e-mail and pay with Visa or MasterCard.

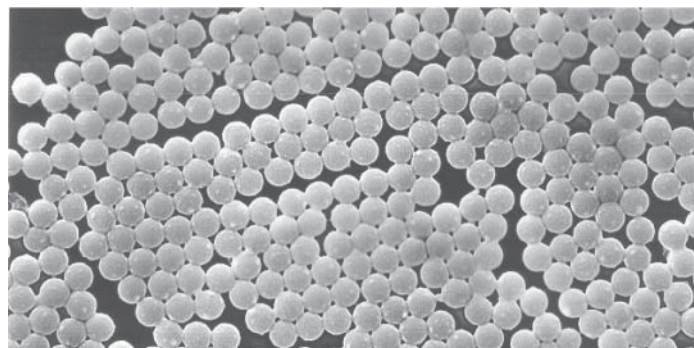
### Beware: Freezin' Season!

During this season we take all precautions to prevent freezing of your microspheres in transit. We ship by overnight transport in insulated packs and avoid Friday shipments. (And it's always a good idea to keep our products refrigerated, but avoid freezing which can destabilize the beads.)



## New Product Developments

estapor® *really* Narrow Distribution Magnetic Beads



We now have 3 lots to show you of some new, very uniform 2-3 $\mu$ m diameter, superparamagnetic beads with 15-20% magnetite.

More New estapor® Stuff (ask for details, if interested)

- ~1 $\mu$ m magnetic fluorescent beads
- 150 nm classical magnetic beads: small and highly carboxylated
- 85-95 nm *surfactant-free* CML (CML = COOH modified latex)
- 140 nm high density (1.2 g/ml) CML beads: high density for easier washing. High COOH (>400  $\mu$ eq/g) = high protein binding capacity
- fluorescent beads with excitation >650 nm: unusual dye

← "No worries, Mate!" (Australian) = "Not to worry!" (American) = "We are here to help you find the particles or microspheres you need— or we'll make them for you." (Bangs Labs/FCSC) And it won't cost you billions. (Cartoon reprinted with special permission from Sidney Harris.)

Ask "The Particle Doctor®":

*Binding Protein to Mag Beads for Ab Fishing*

**Q:** How do I bind a protein, via the protein's carboxyl or amino terminus, to 2-5  $\mu\text{m}$  magnetic beads and then use these beads for pulling out antibodies that bind to the protein? (I don't want to use a chemistry that might modify the cysteine residues on my protein.) Also, would it be easier to use preactivated beads that I can just react with my protein so I don't have to do the chemical reactions myself?

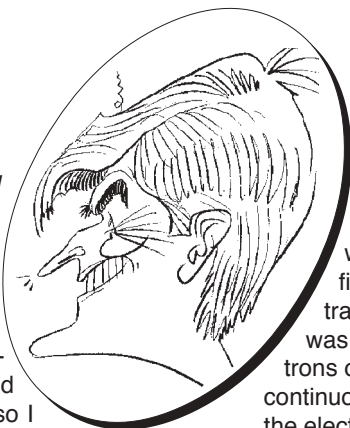
**A:** *You folks keep sneaking in two questions. OK this time.*

1) To avoid the possibility of binding to the cysteine residues on the protein, try our COOH-functionalized mag beads. Activate the beads with EDAC and NHS; wash the microspheres; and add protein. Unlike the o-acylisourea intermediate formed by EDAC reaction, the succinimidyl ester formed by the NHS will not react with thiols. (See also our TechNotes #205 "Covalent Coupling" and #102 "Magnetic Microspheres.") 2) Our largest magnetic microspheres are 2-3  $\mu\text{m}$ . A suitable product that is available for immediate shipment is as follows: #3240, 2.29 $\mu\text{m}$  P(S/V-COOH) Magnetic Encapsulated (22% mag.). Pricing is \$243 / 0.5g. Orders may be placed through our website or by contacting our Customer Service Department. 3) If you can biotinylate your protein, then you could choose our streptavidin-coated ProActive® mag beads. (Ask if you need help.) *Thanks to our secret weapon, Kathy Turner, for the answers.*

*Binding Concanavalin to Beads*

**Q:** As a complete novice to beads, I would like some advice on how to coat them with Concanavalin A. Passive adsorption? On what kind of beads? Or is covalent coupling a better option?

**A:** *Wow, three questions this time!* For general advice on handling beads and especially covalent coupling vs. adsorption see TechNote #201, "Working with Microspheres." Passive adsorption on PS beads works best with larger proteins, like IgG, which stay adsorbed; otherwise, try COOH-modified beads and EDAC coupling. (See TechNotes # 204, "Adsorption..." & #205, "Covalent Coupling.")



**SiO<sub>2</sub> Beads Vital Links in Global Fiberoptics Net**

If you ever wondered how they link all those miles of optical fiber cables together, then read on. (If not, then, "Sorry to bother you!") Phone companies and communications networks are stringing thousands (maybe millions?) of miles of fiberoptics all over the world to carry phone messages and transport data faster than old-fashioned copper wire. The wire was soldered together at joints or switching points, so the electrons could flow from Anchorage to Zanzibar and back through a continuous metal path—and it didn't need to be a straight path, since the electrons didn't care about bends.

So how do they link fiberoptics together? What kind of joints let light flow in those "light pipes" they call optical fibers or fiber optics? Well, you'll remember from school that light waves flow in straight lines, so special care must be taken to link the light pipes up end to end so the light keeps flowing straight or smoothly in those "pipes."

It turns out that the optical engineers at places where they make and use optical fibers found that when they put the light fibers end to end they didn't always get a good connection (maybe improper alignment of the fibers or inefficient light transfer from the end of one fiber to the other fiber. But, when they put a tiny glass or silica microsphere or bead (about the same size as the fiber) in the gap between the ends of the fibers, they got good optical alignment and more efficient light transfer.

Well, Bangs Labs makes uniformly sized silica (like glass) microspheres or beads in sizes up to 5 micrometers (microns) in diameter. Since there are about 8 billion microspheres per gram of the 5 micron microspheres, each gram of microspheres will permit many, many fiberoptic connections. And we make the beads in multiple kilogram batches, so there isn't any danger of a shortage soon. We are very proud to be helping to connect the world via optical fibers. (Think of us when you make a phone call.)

**Mail Bonding (Subscribers "do the 'write' thing!")**

❖ "Your streptavidin-coated magnetic microspheres performed better than equivalent products from three other suppliers. I also have had very good luck with your streptavidin-coated silica microspheres, but the web site says they're not available. Will they be available soon?" (KP, Australia) Thanks for valuable feedback. SA-silica is available again. Check out our web site for choices.

❖ "Your sales reps. know their stuff and they are very helpful." (JK, CA) Shhh! If they hear that, we'll have to start paying them.

❖ "I like your website and your sense of humor." (I.C., New York City) I'm happy to hear that someone appreciates our attempts.


Please remember BLI for... **BEADS • ABOVE THE REST™**

*Righ B. Bangs*, The Particle Doctor®

**Have a Holly, Jolly \_\_\_\_\_ (whatever you call it)!  
It's the Best Time of the Year!**

At this time of year we think of all the folks who are important to us. It is our continuing goal to be the best supplier of microspheres in the world, and we really appreciate your support of our efforts. Without you (*the best customers in the world*) we could NOT survive, and we know it. Please accept our sincerest best wishes to you and yours from everyone at BLI for a joyous season (however you celebrate it). May Y2K + 1 be your best year ever! And do let us know how we can help you to be more successful. We hope that you enjoy the enclosed calendar. It can be stuck on your computer monitor or keyboard for quick reference throughout all of 2001.

**Make it idiot proof and someone will make a better idiot. Anonymous Bumper Sticker**

Technical References— See our website ([www.bangslabs.com](http://www.bangslabs.com)) for “downloadable” TechNotes and papers (marked  below), or ask for copies by mail or fax. We continually update and add newest TechNotes to our website.

**Product-Specific TechNotes (100 Series):**

101. *ProActive*<sup>®</sup> Microspheres—Handling tips + protocols for streptavidin, Protein A, and goat anti-mouse coated microspheres. (08/99)
102. Magnetic Microspheres— Data + handling tips for >11 varieties of *estapor*<sup>®</sup> superparamagnetic particles 0.7-1.4  $\mu\text{m}$ ; COOH and NH<sub>2</sub>-modified; classical, encapsulated (low surface iron content), etc. (08/99)
103. Fluorescent/Dyed – Applications, fluorescence spectra, and product list. Includes confocal microscopy standards. (08/99)
104. Silica Microspheres – For immunoassays, nucleic acid capture, velocimetry (LDV, PIV), flat panel display spacers, others. (08/99)
105. NIST-Traceable Standards – Data for 9 sizes (0.2–20 $\mu\text{m}$ ), available singly or in kits, with certificates of analysis. (08/99)
106. Confocal Standards – Using our three, bright, single-label 63 nm fluorescent beads in confocal microscopy. (08/99)

**Handling-Specific TechNotes (200 Series):**

201. Working with Microspheres – Choosing, cleaning, characterizing, coating beads, etc. (L.B. Bangs 2nd lecture at *The Latex Course*<sup>TM</sup> 5/99)
202. Microsphere Aggregation – Preventing, detecting, and reversing aggregation. Chemicals and equipment sources (08/99)
203. Washing Microspheres - Protocols for different methods for cleaning microspheres; advantages/disadvantages of methods; suppliers of equipment. (08/99)
204. Adsorption to Microspheres – Adsorbing proteins onto particles; use of “surface diluents” (blockers); recipes and references. (08/99)
205. Covalent Coupling – Chemical attachment of proteins to 8 types of surface-functionalized microspheres; recipes for buffers, blockers; misc. coupling ideas, vendor information, and references. (08/99)
206. Useful Equations – For calculating particles/ml, area/g, “parking area”, settling velocity @ 1G and in centrifuge, etc. (08/99)
207. *ProActive*<sup>®</sup> Streptavidin Coated Microspheres and Their Binding Capacity for Biotin and Biotinylated Oligonucleotides – K. Turner, 2000 AACC OEM Lecture Slides (09/00)
208. Microsphere Sizing – Various manual and automated methods are described and discussed, with references and supplier list. (02/00)

**Application-Specific TechNotes (300 Series):**

301. Immunological Applications – Review of commercial applications of microspheres. (L.B. Bangs 1st lecture at *The Latex Course*<sup>TM</sup> 5/99)
302. Molecular Biology – Expanded overview of purification and solid phase separation methods. (08/99)
303. Lateral Flow Tests – putting dyed particles on membranes so they will move properly. (08/99)
304. Light-Scattering Assays – Turbidimetric and nephelometric applications of microspheres. (08/99)

**Reprints (400 series):**

401. *estapor*<sup>®</sup> “Microspheres” booklet – 1995 revision: Information on fluorescents, encapsulated and narrow magnetics, nanoparticles (<50 nm), NIST-traceable standards; many handling tips; >60 references.
402. Microspheres, part 1: Selection, cleaning, and characterization, and part 2: Ligand attachment and test formulation—LB Bangs & Mary Meza, *IVD Technology (in Medical Device & Diagnostic Industry)*, 17, #3, 18-26, March, and #4, 20-26, April, 1995. (Note that you can download these papers at the IVDT website: [www.devicelink.com/ivdt/archive/95/03/009.html](http://www.devicelink.com/ivdt/archive/95/03/009.html) and [.../95/04/006.html](http://www.devicelink.com/ivdt/archive/95/04/006.html))
403. New Developments in Particle-Based Immunoassays: Introduction - Leigh B. Bangs, *Pure & Appl. Chem.*, 68, #10, 1873-1879 (1996) Review of 40 years of diagnostic uses of microspheres—from LATs to biosensors.
405. Applications of Magnetic Particles in Immunoassays - Mary Meza, Ch. 22 (pp. 303-309) in *Scientific and Clinical Applications of Magnetic Carriers*, Håfeli, U, et al., Eds, Plenum Press, New York, 1997.
406. Measuring microsphere binding capacity – JM Duffy, JV Wall, MB Meza, LJ Jenski, *IVD Technology*, 4, #7, 28-34 (1998). (No reprints are available; you can download from our website.)
407. Bead-based HTS applications in drug discovery - MB Meza, *Drug Discovery Today: HTS supplement*, 1, #1, 38-41 (2000).

Meet Prof. Quanty! See the FCSC website ([www.fcstd.com](http://www.fcstd.com)) for lots of technical information about flow cytometry standardization in general and our new flow cytometry standards products in particular.

Free Literature Exchange! What information do you need? We'll share our library: ~1000 papers about microspheres, cross referenced, so we can search for types of particles, coupling methods, uses, author, etc. New papers are added as we get them. No cost to you. All we ask in return is that you tell us about good papers which we should have as you find them. And we'll even offer to send you a small reward for new references!