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New Developments in High Performance Magnetic Separation Technology for Laboratory and Industrial Applications

David Humphries, Martin Pollard

D.O.E. Joint Genome Institute/

Lawrence Berkeley National Laboratory

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Emerging Magnetic Technology for Genomic, Proteomic and Bio-Medical Applications

- Hybrid 384-well magnet plates for molecular separation
- Hybrid 96-well magnet plates
- New development areas from deep well plates to single molecule manipulation
- Technology transfer and industry collaboration

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Unique Technology with Broad Applicability

- New class of magnet plates developed at JGI/LBNL for high-throughput purification of biological samples in high-density microtiter plates
- Technology can selectively separate proteins, DNA and other molecules from various contaminates based solely on a magnetic field
- Magnetic structure is a unique hybrid of permanent magnet and ferromagnetic materials that produces magnetic fields significantly stronger than those of commercially available magnet plates

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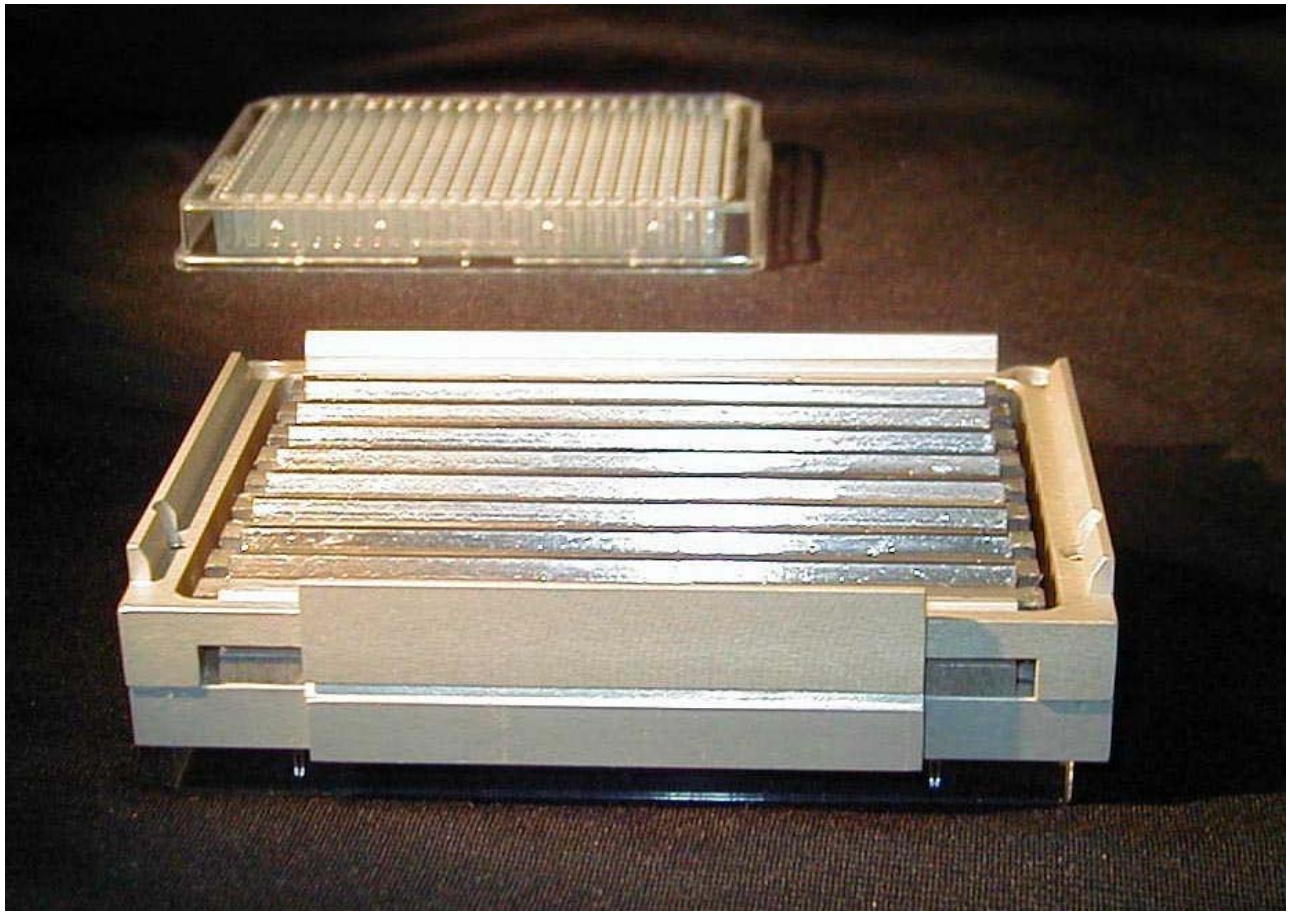
Hybrid Magnet with Plate Interface and 384-Well Microtiter Plate



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High Throughput and Benchtop Use

- Hybrid magnetic structures are currently an enabling technology for sequencing approximately 2.5 Gigabases of DNA per month at the DOE Joint Genome Institute.
- Hybrid magnet plates have been developed for general bench top use in addition to automated high throughput applications.

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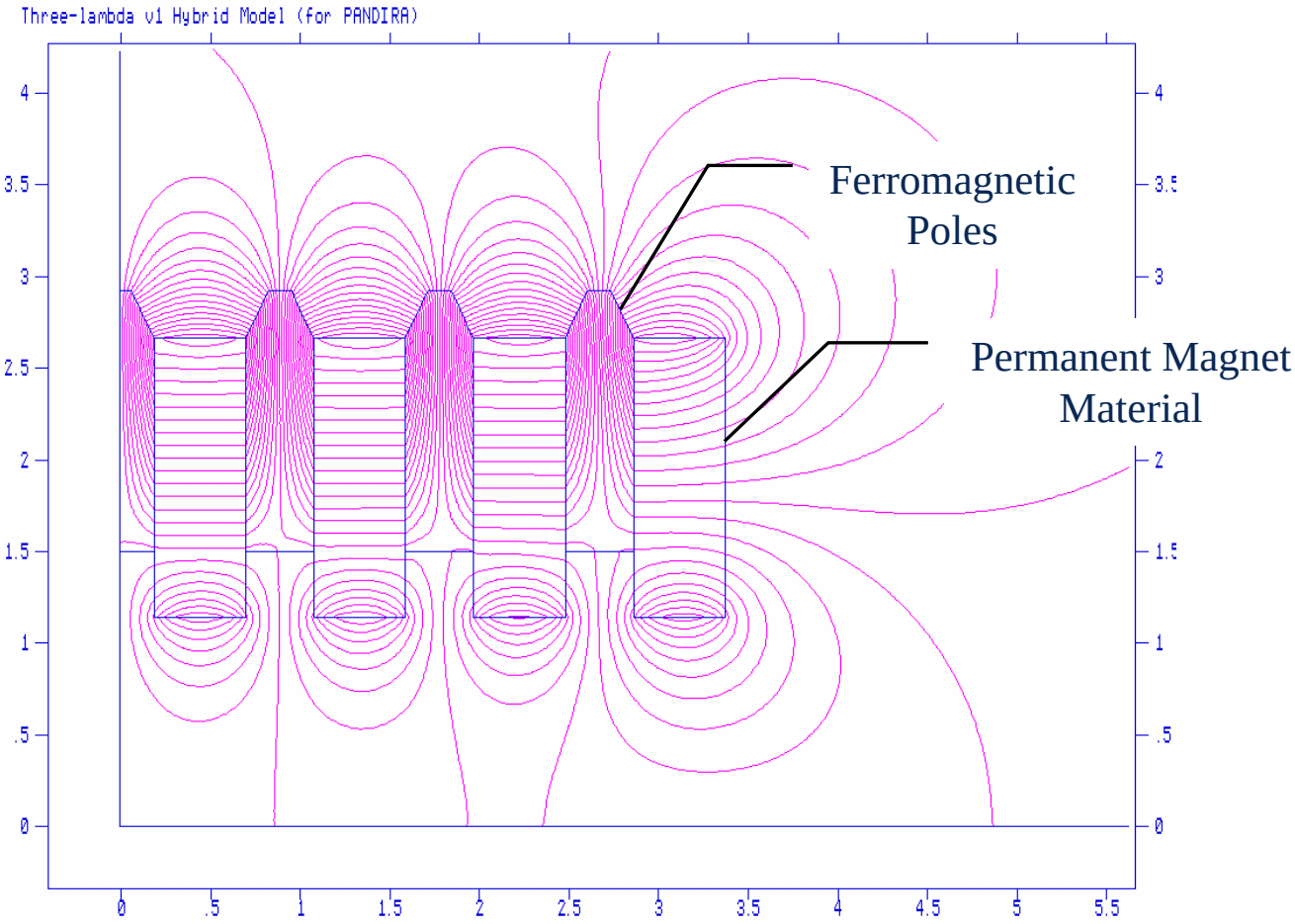
Computer Model of Hybrid MagneticStructure



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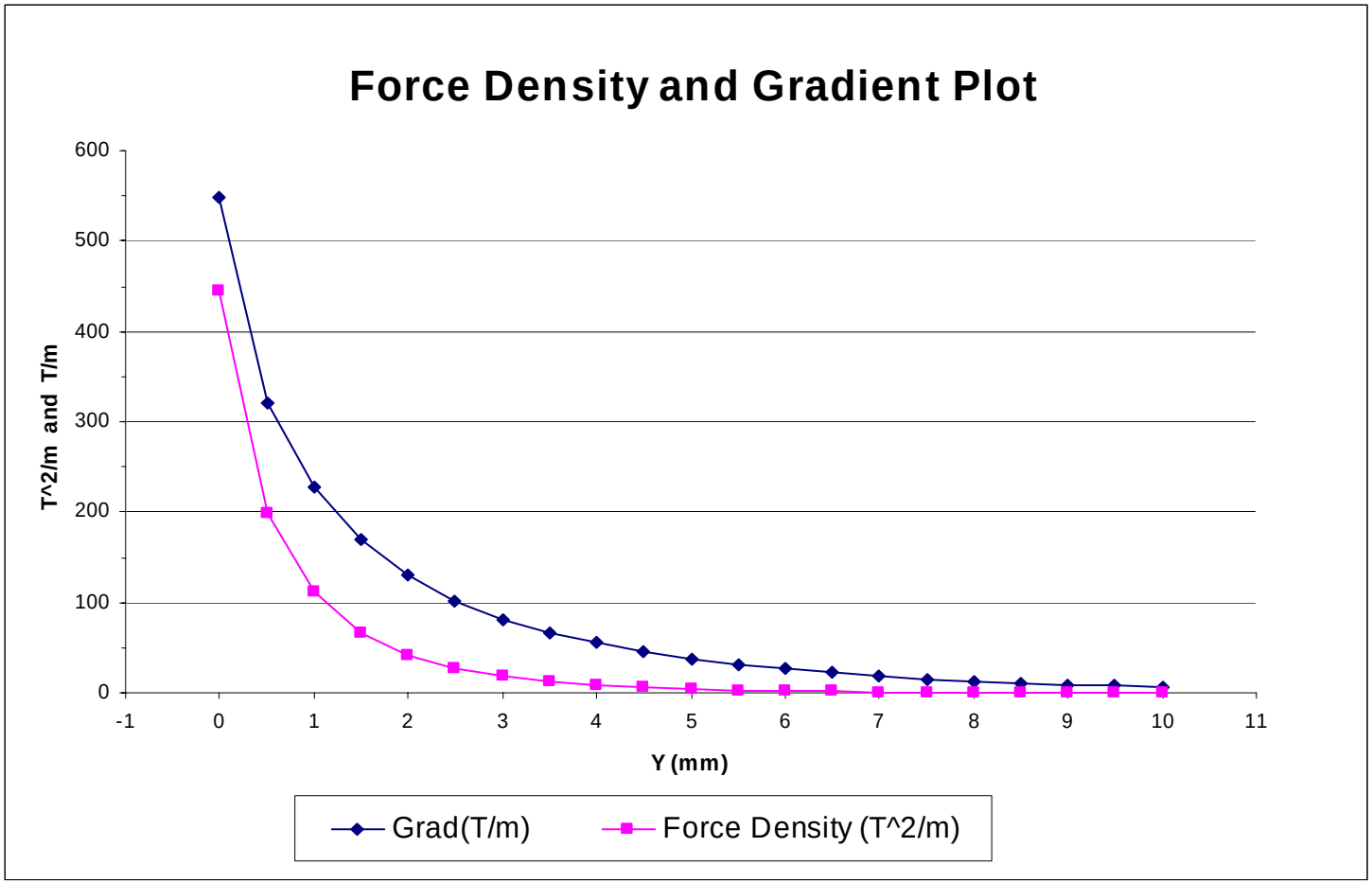
High Fields and Strong Gradients



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Target Species Are Magnetized

- Magnet plates work in conjunction with 0.5 to 5.0 micron magnetic beads
- Beads are attached to DNA or other targets such as proteins by means of specialized bead coatings
- Various bead types are commercially available

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Applications

- Functional genomics
- Genetic sequencing
- Proteomics
- Immunological drug screening
- Automated DNA purification
- Automated protein purification
- Any magnetic bead based purification method
- Single molecule manipulation

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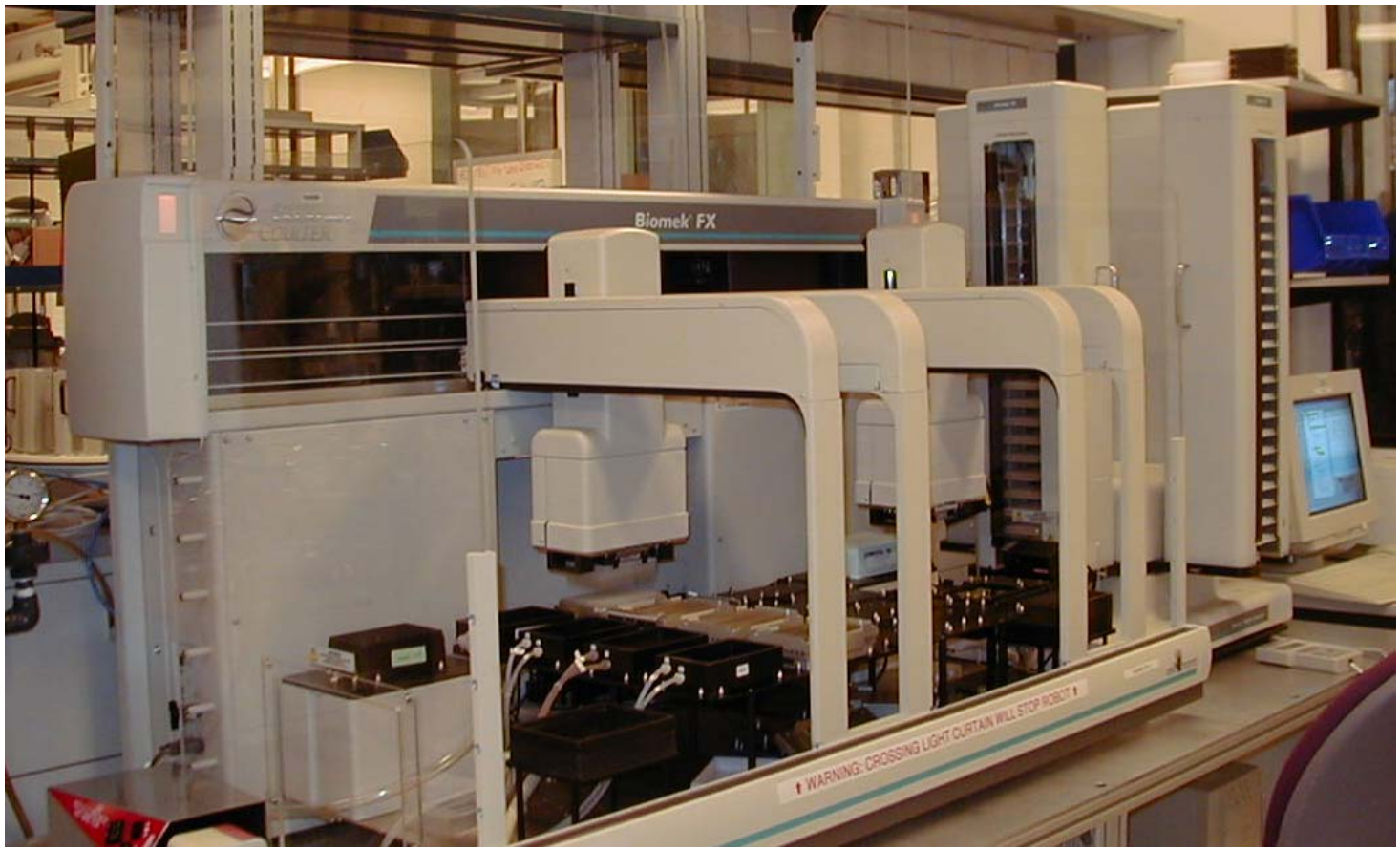
BiomekFX Liquid Handling Robot with Four Hybrid Magnets Installed



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Close-up of Hybrids on Biomek-FX Deck

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Advantages of Hybrid Technology

- Fields are 70 to 100% stronger than that of the best commercial magnet plates measured
- Produces higher sample yields and faster processing times
- Greater holding power means more robust process
- Compatible with most 96, 384 and 1536-well standard microtiter plates

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General Attributes

- These hybrid structures are energized by permanent magnets and require no external power source
- They are compact, with a footprint slightly larger than a standard microtiter plate and a thickness of approximately 1 to 1.8 inches
- Documented fabrication techniques have been developed that allow for high quantity/quality production of these structures

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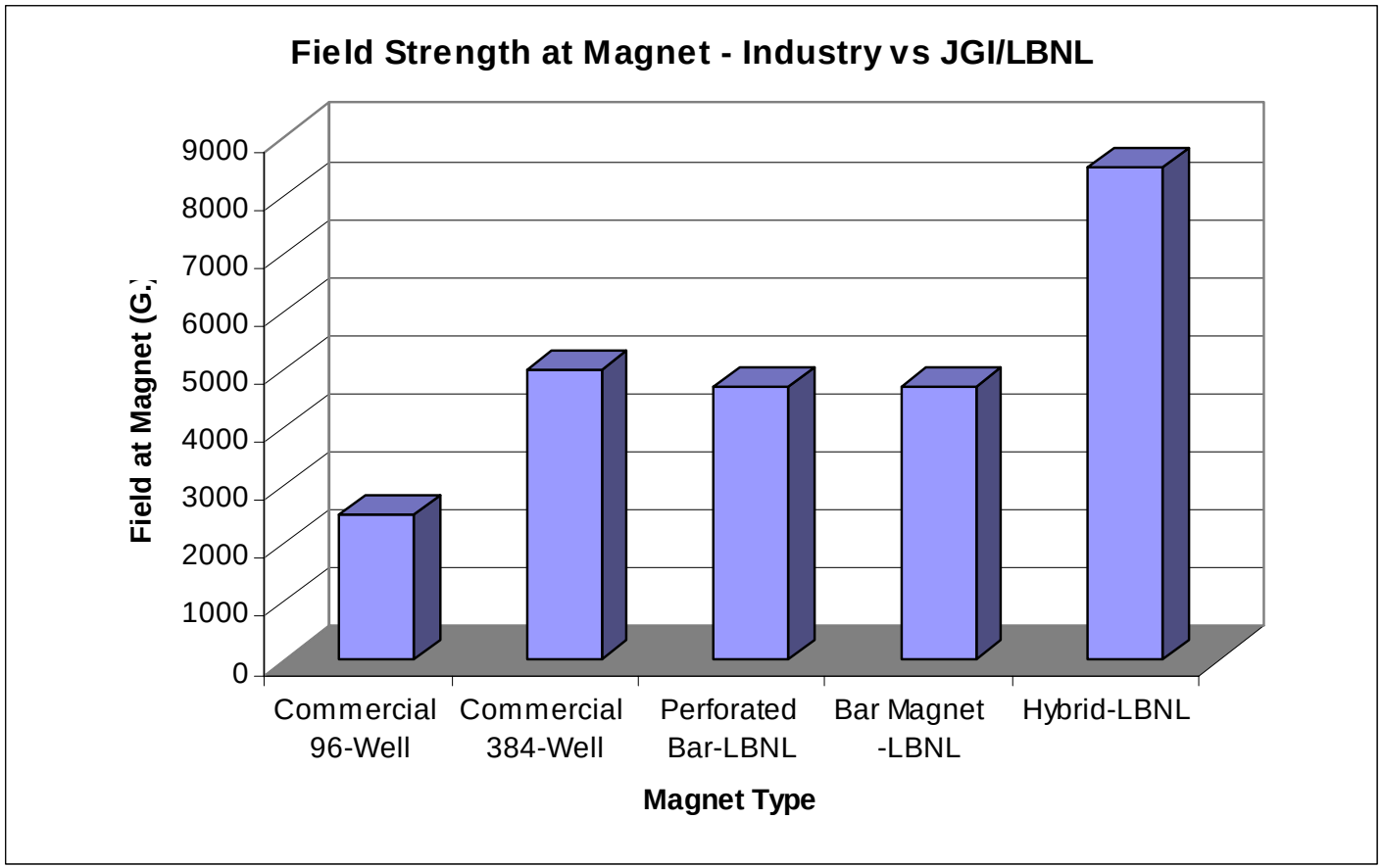
Performance Comparison

- Relative field strengths of five different magnet plates were compared.
- Three of the magnet plates were developed at JGI/LBNL.
- The other two magnet plates are commercially available models.
- The field strengths were measured at two heights: (a) at the magnet surface and (b) at 1 cm above the magnet surface.
- Measurements were made using a Hall effect probe.

Fields at magnet surface are 70% greater than industry 384-well magnet plates tested



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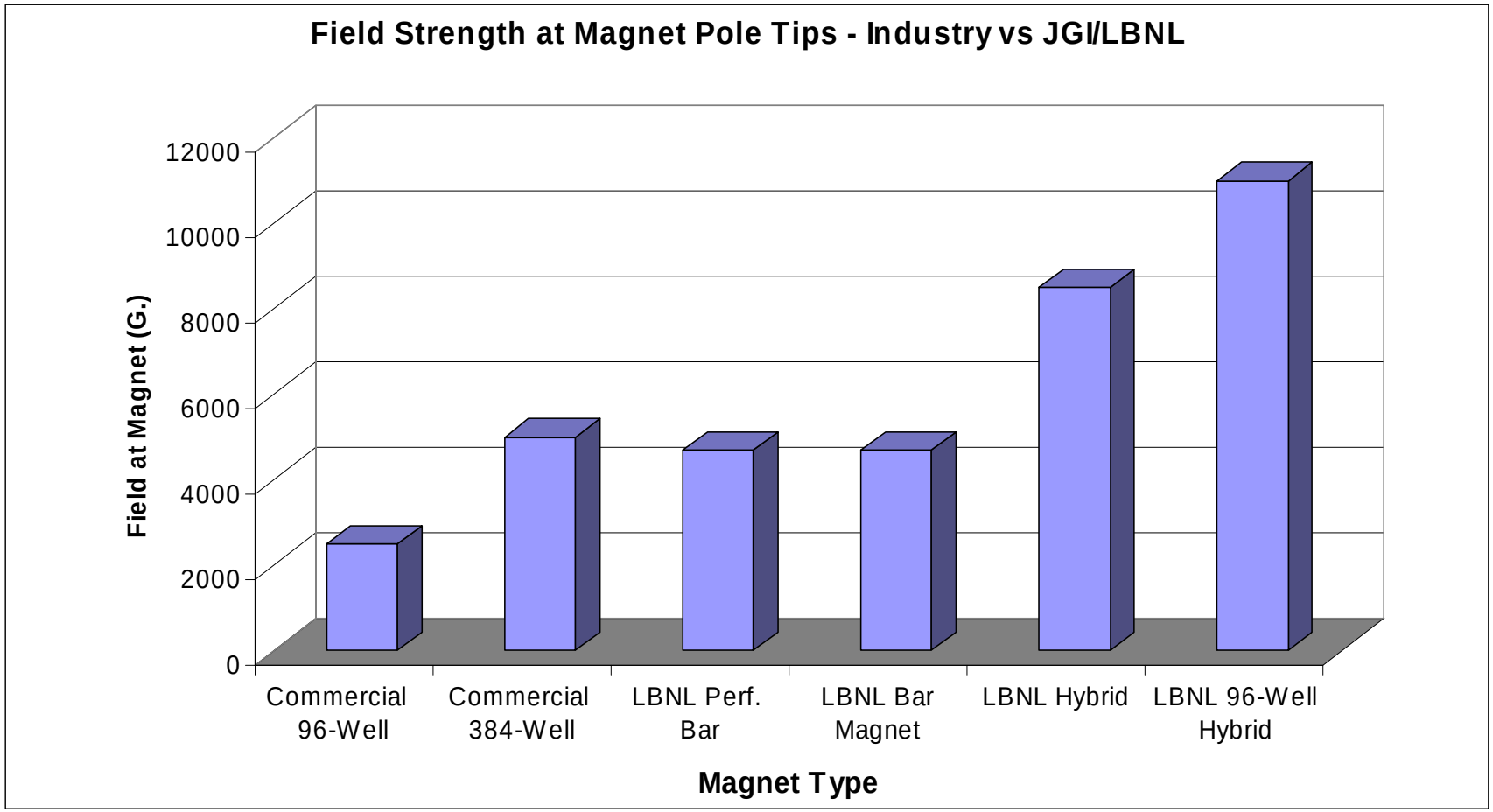
Fields at magnet surface are 70 to 100% greater than industry 384-well magnet plates tested



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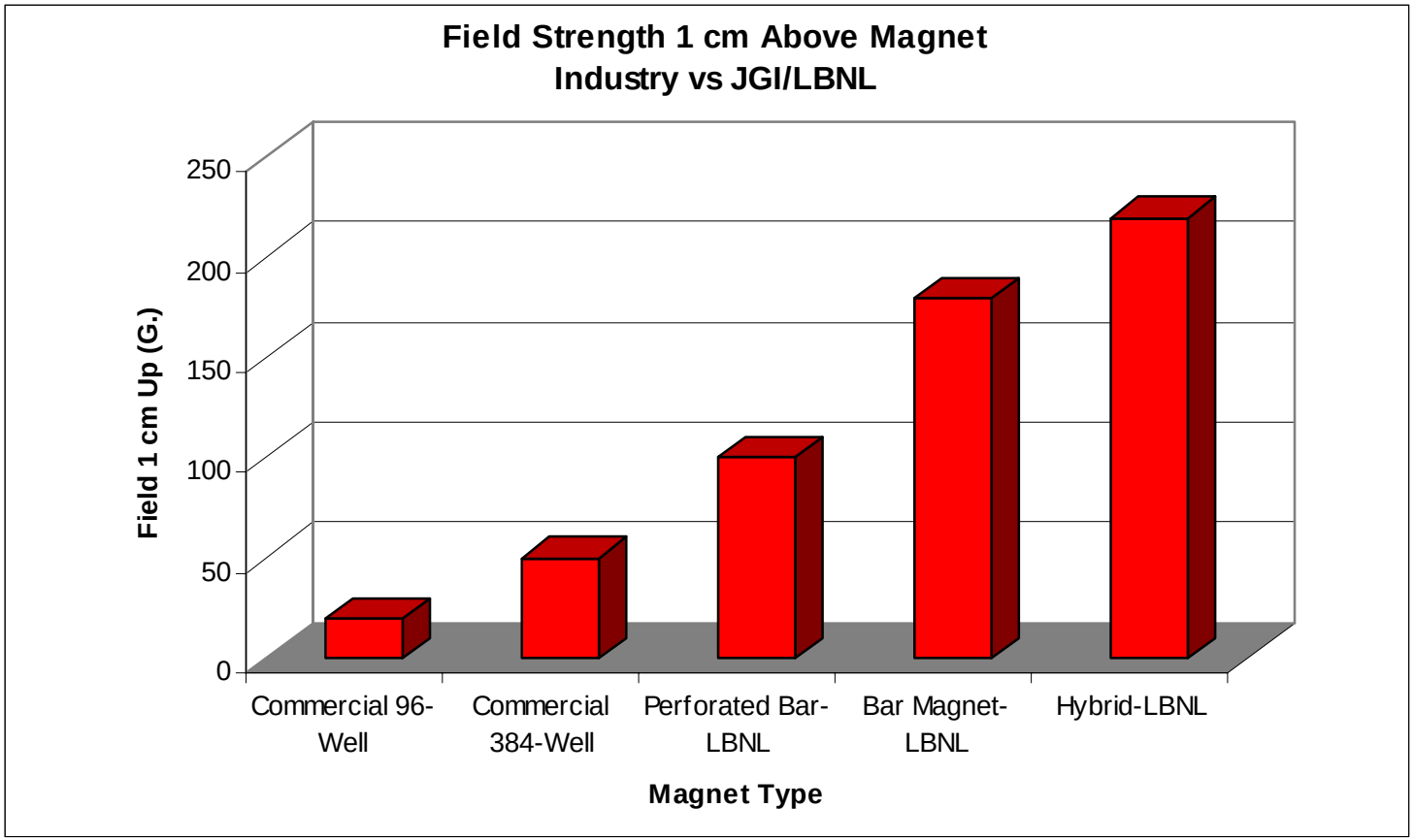
Fields 1 cm above the magnet are approx. 400% stronger than 384-well commercial magnet



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Drawdown Performance Comparison

- Video still sequence provides a draw-down comparison between the hybrid and a common commercial magnet plate
- 1 micron beads are suspended in a viscous solution in 384-well microtiter plates
- Non-magnetic mock-up plate is included for visual reference

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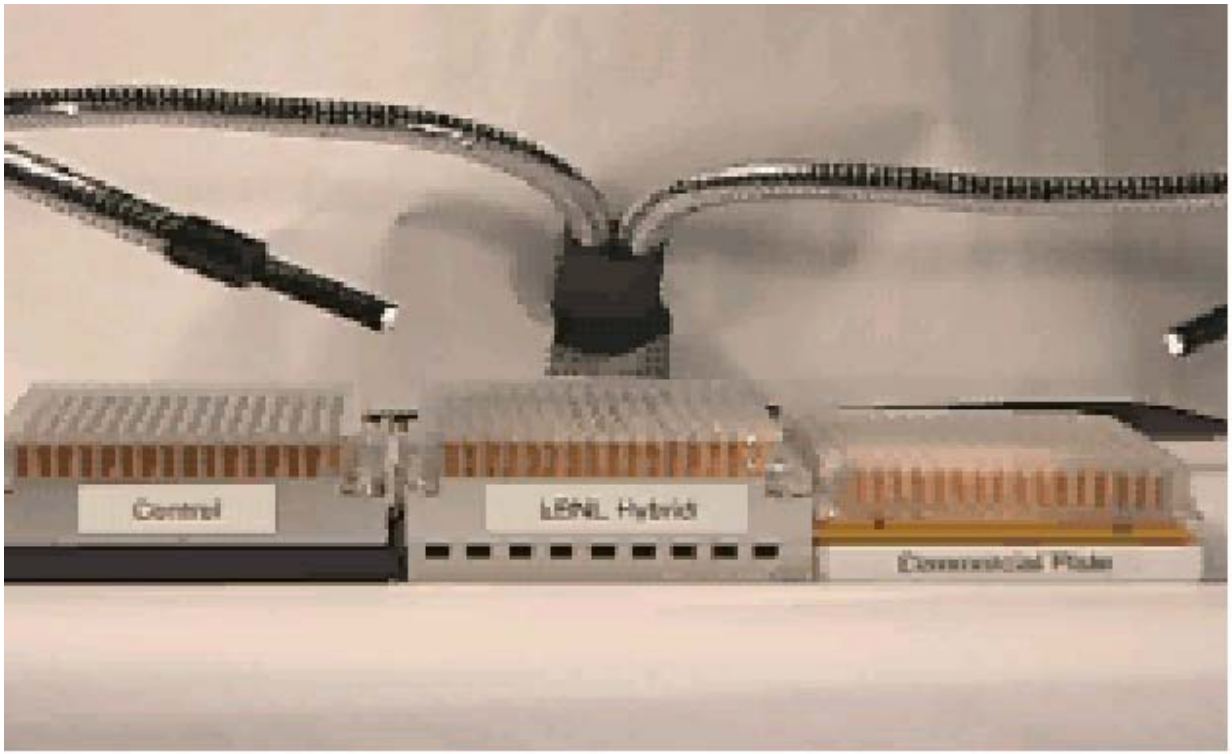
Hybrid vs Commercial Plate - Initial Conditions



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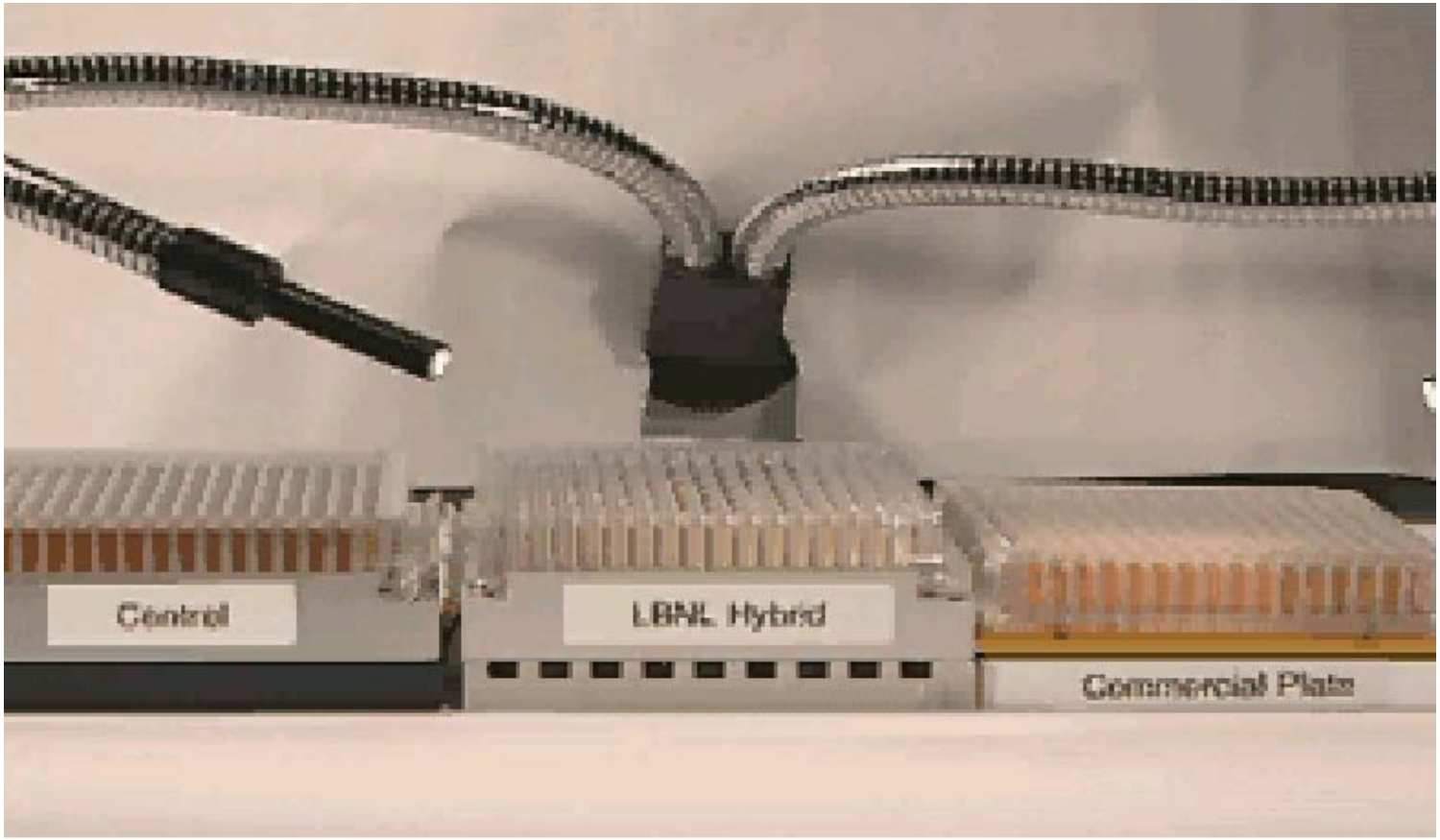
Drawdown After 20 Seconds



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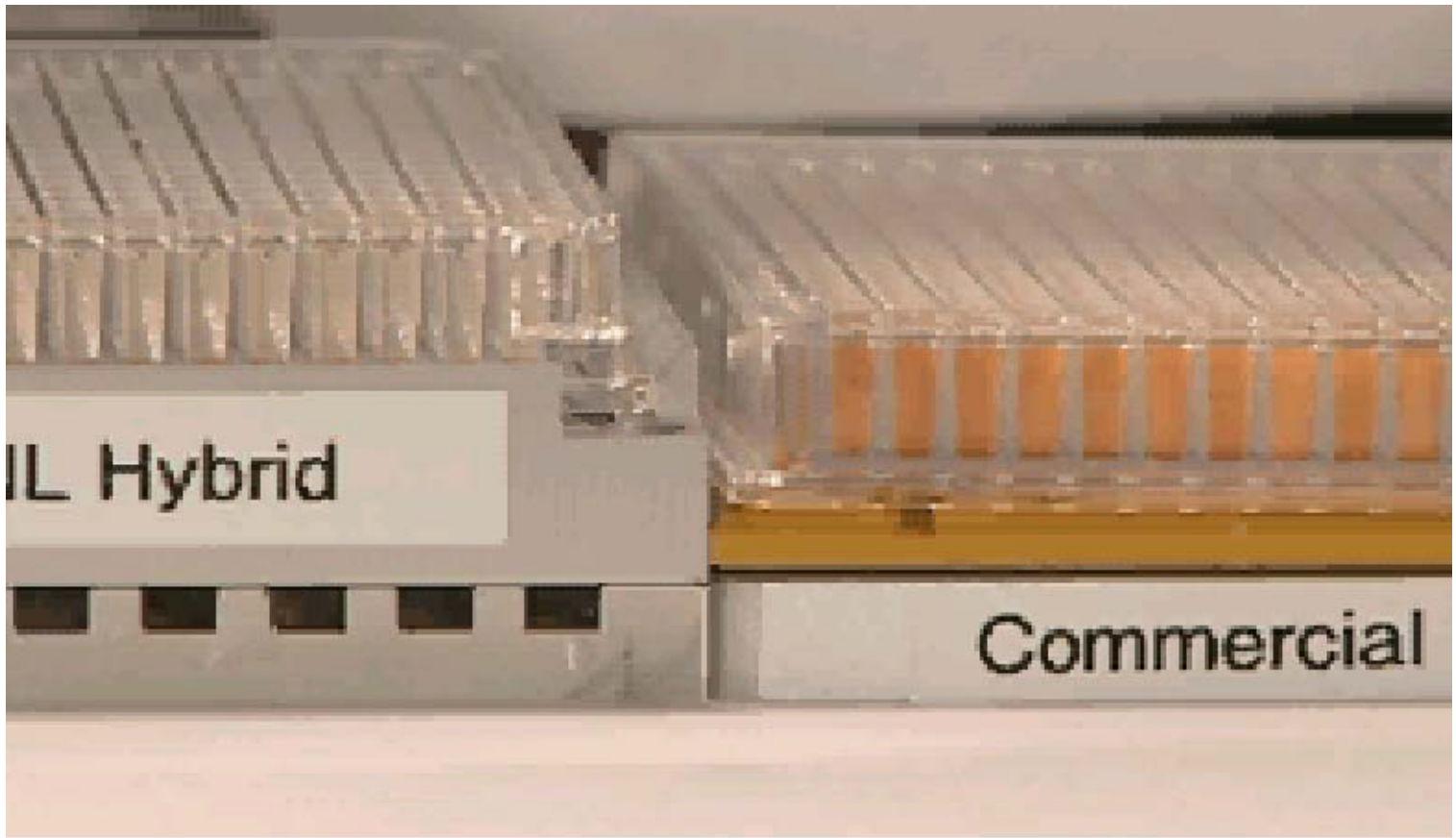
Drawdown After 30 Seconds



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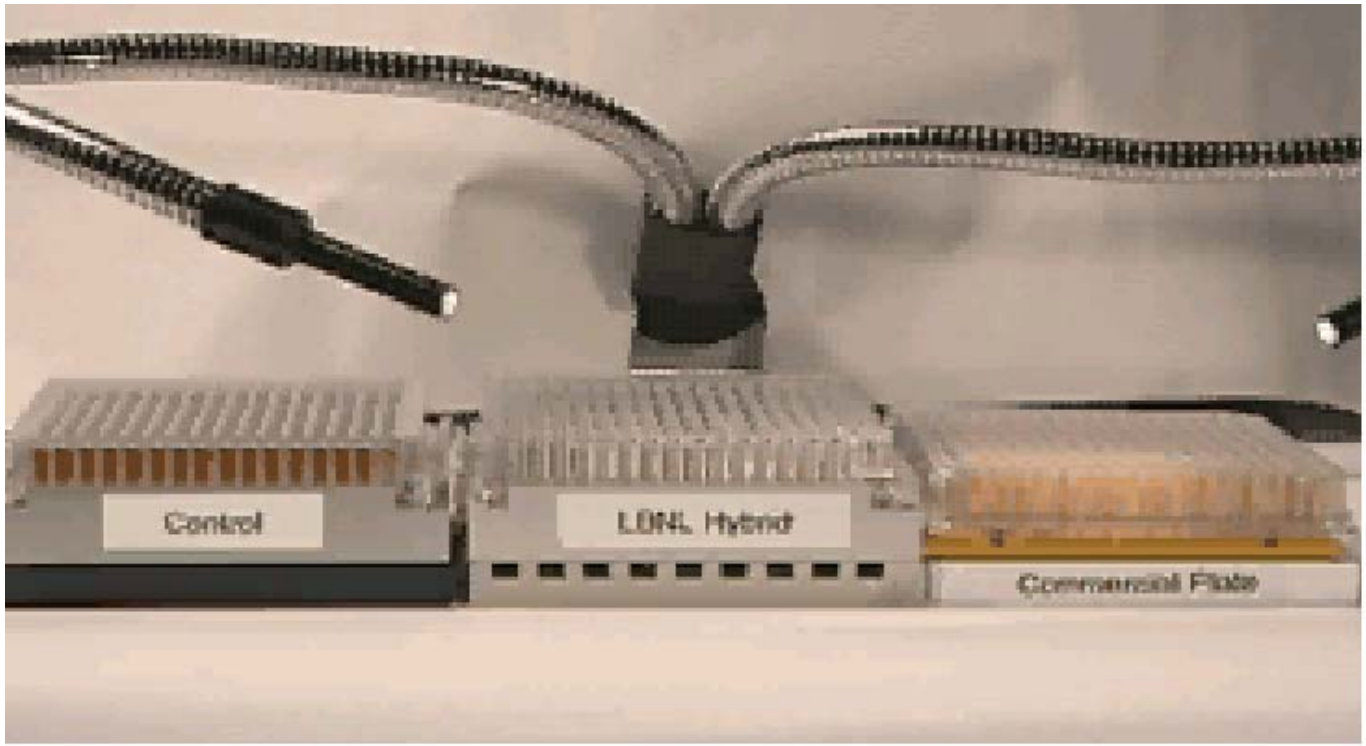
Drawdown After 50 Seconds



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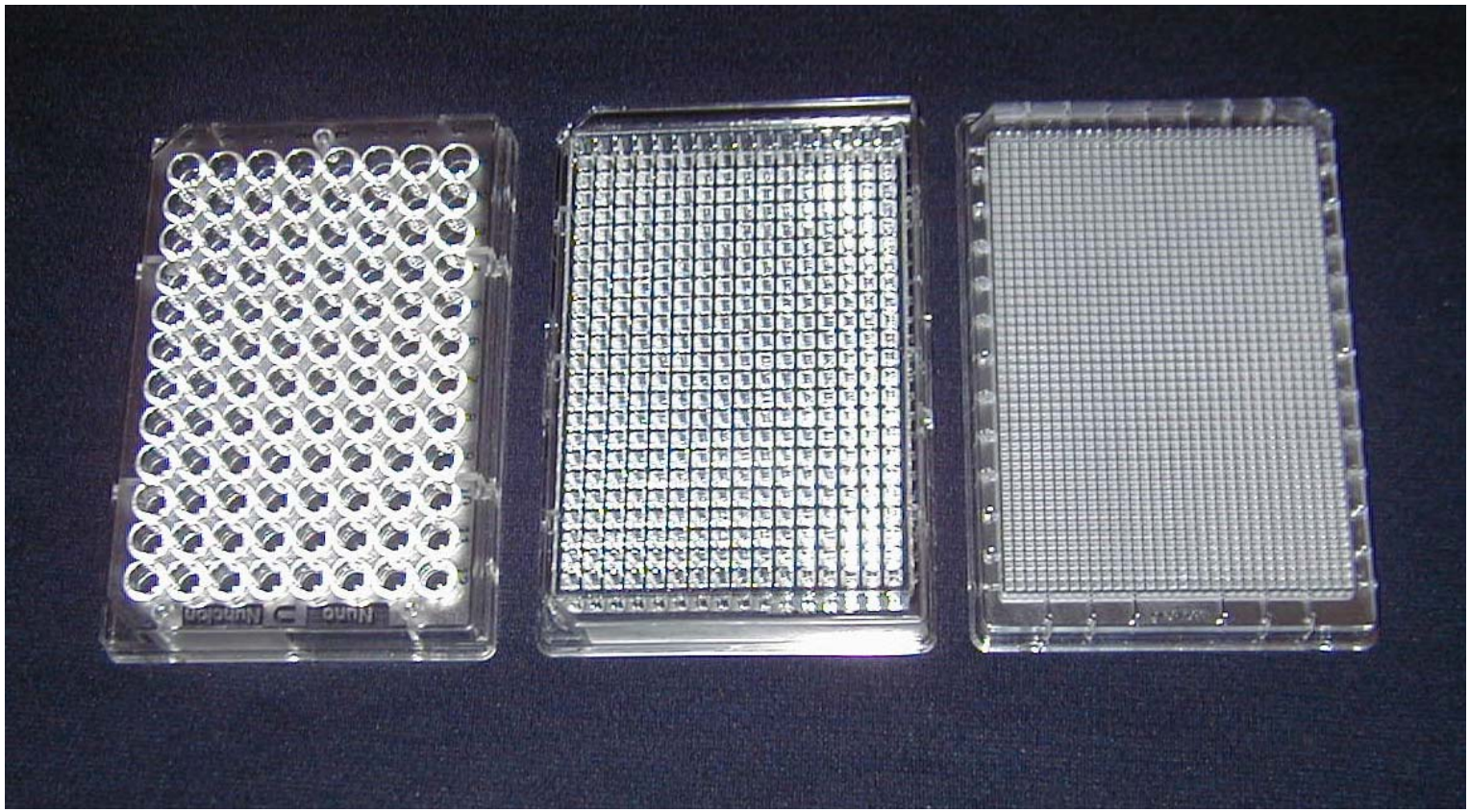
96-Well, 384-Well & 1536-Well Industry-Standard Microtiter Plates



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New Hybrid-96 Prototype Plates In Testing

- Second generation Hybrid structures
- Optimized for higher fields and gradients
- Initial configurations for 96 well microtiter plates
- Designed for fast drawdown and beneficial distribution of targets

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Hybrid 96-well Prototype

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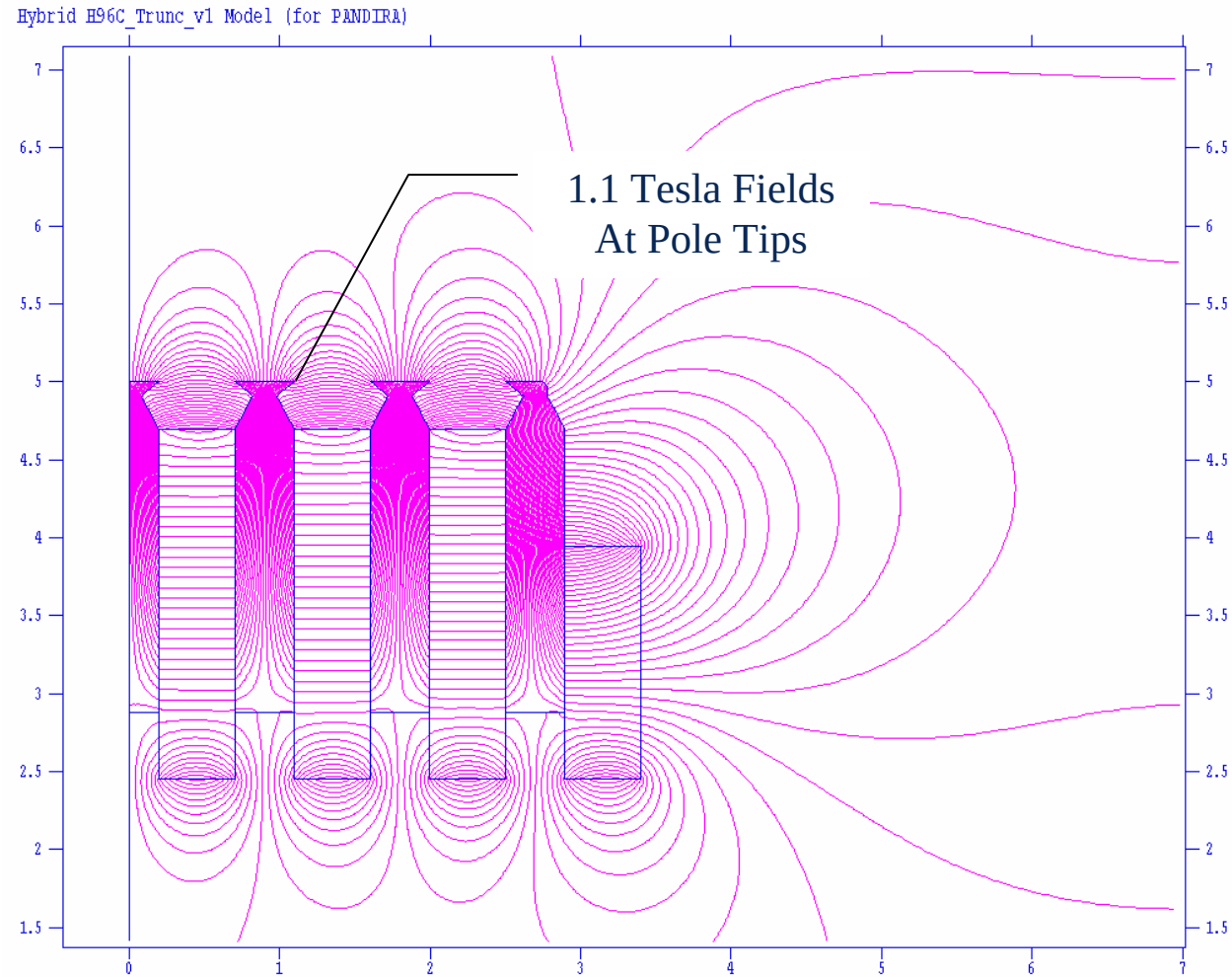
Computer Model of 96-Well Hybrid Fields



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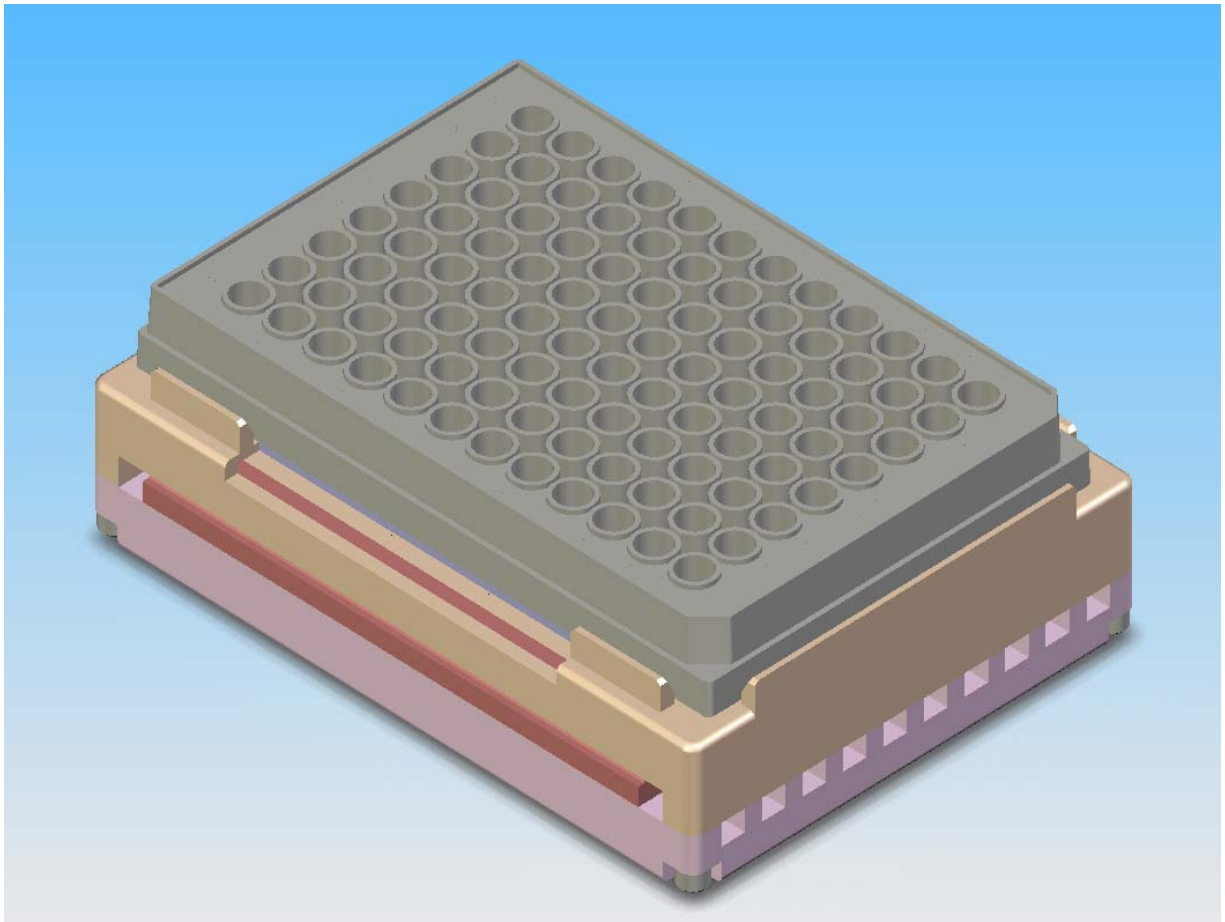
Second Generation 96-well Hybrid Magnetic Structure w/ 96-well Microplate



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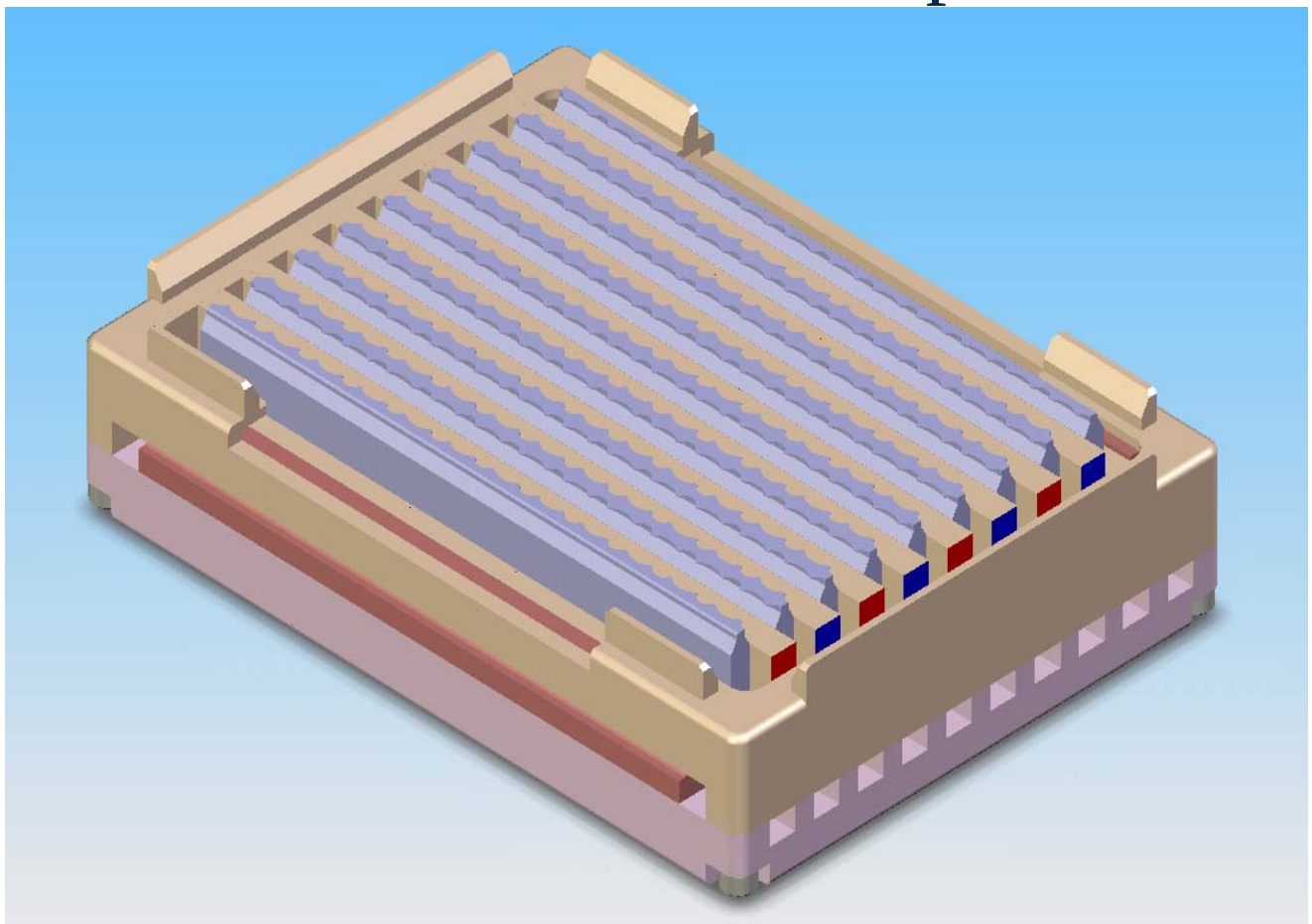
Second Generation 96-well Hybrid Magnetic Structure w/o Microplate



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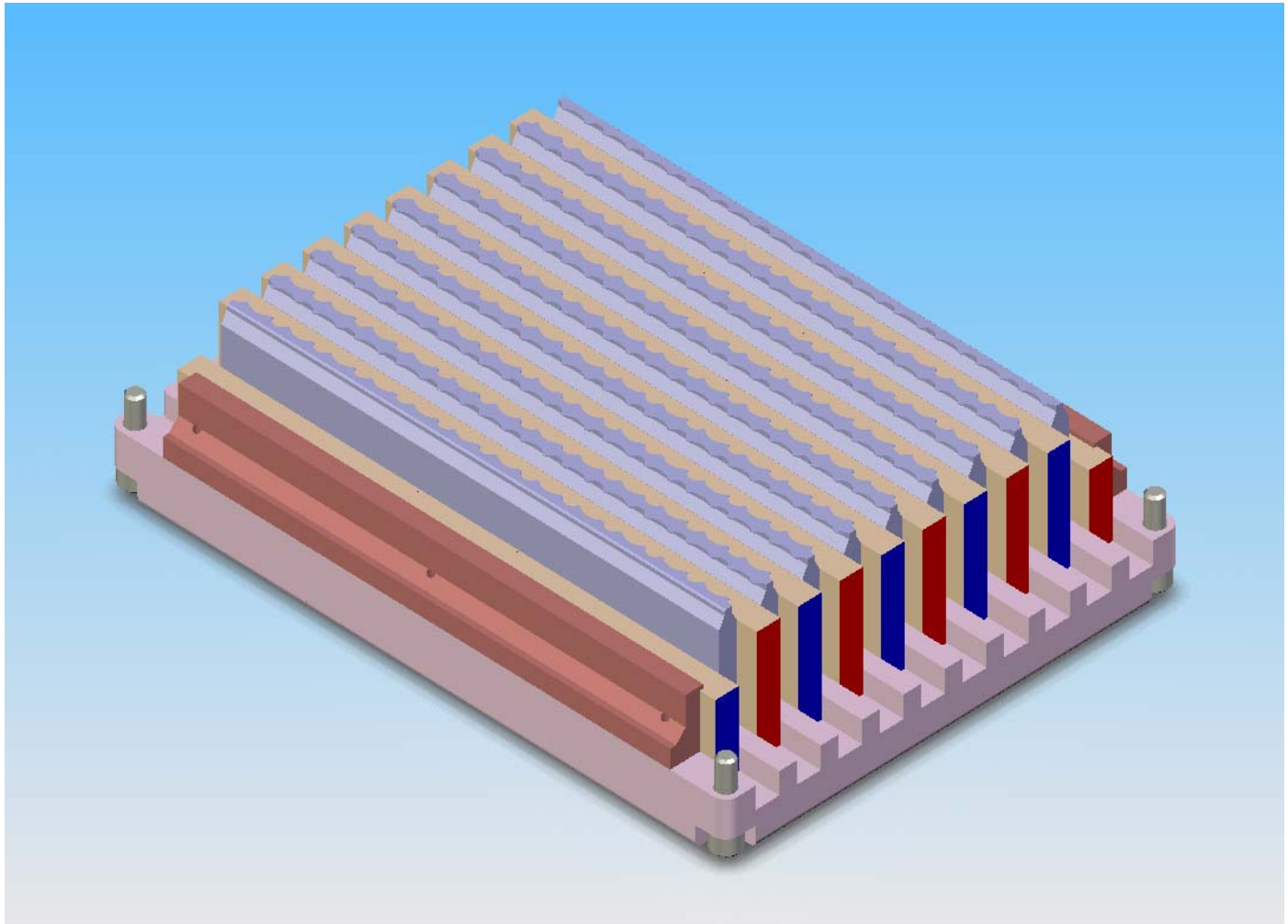
Hybrid-96 Core Magnetic Structure



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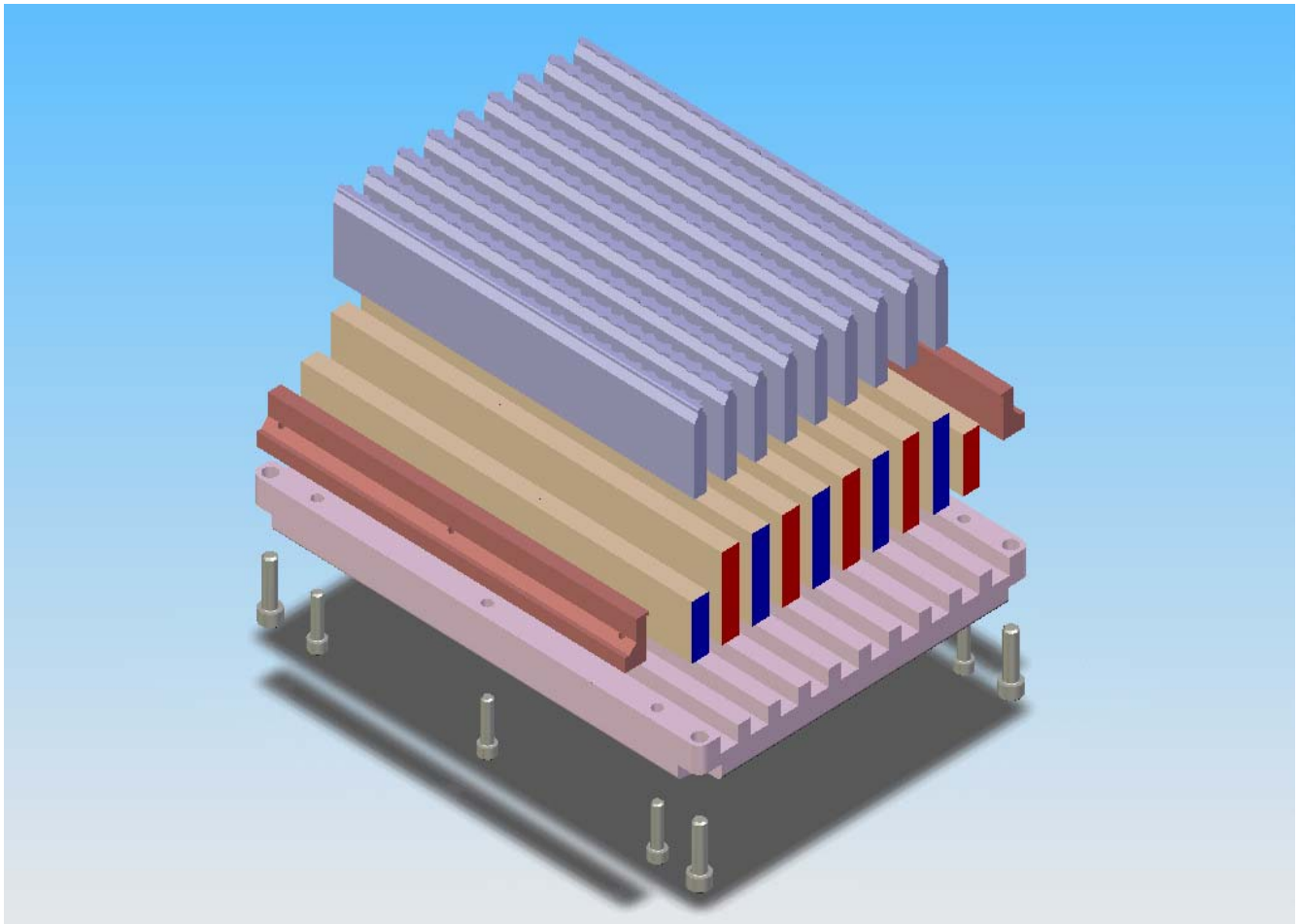
Hybrid-96 Exploded View of Core Magnetic Structure



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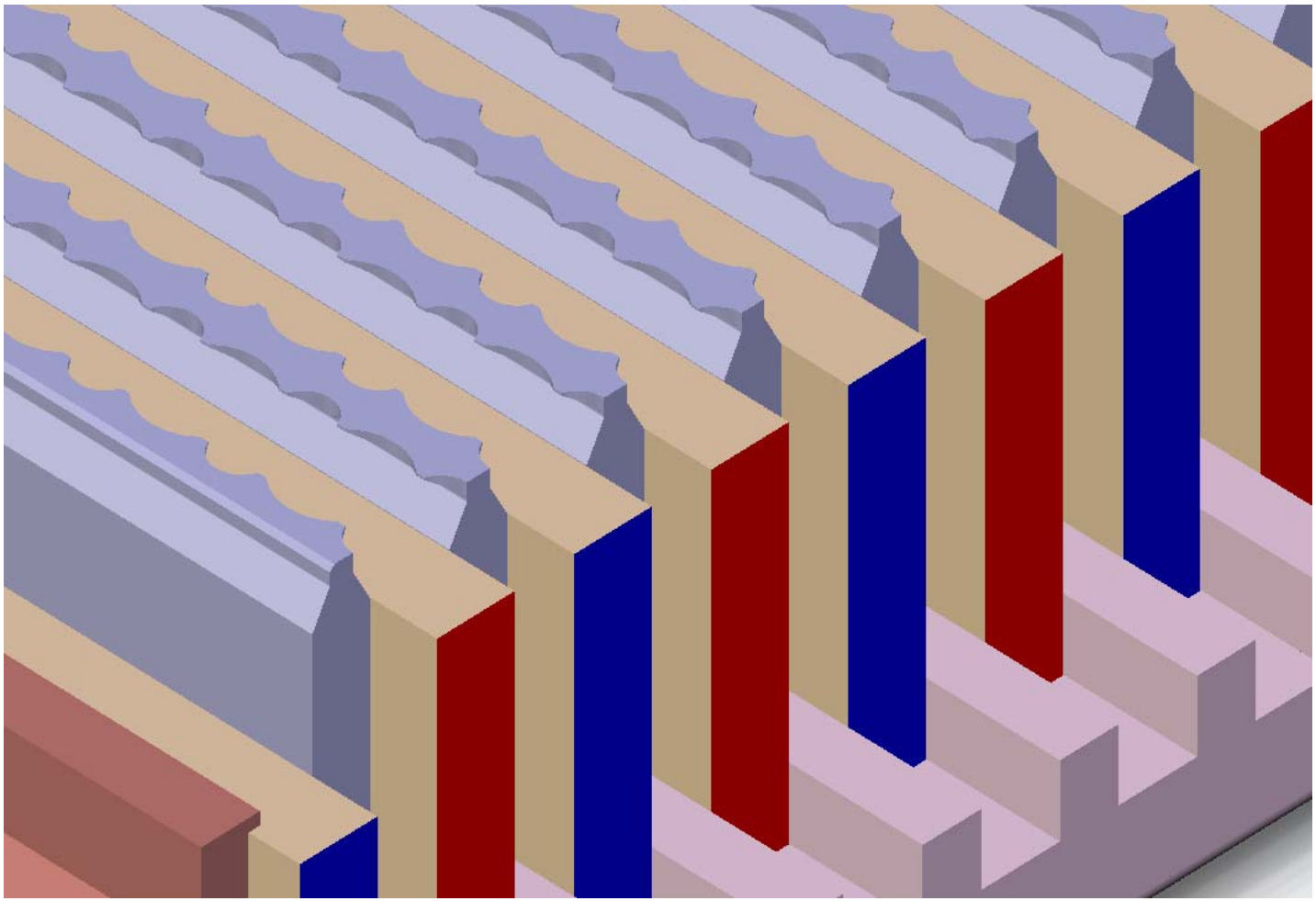
Hybrid-96 Detail View of Pole Tips



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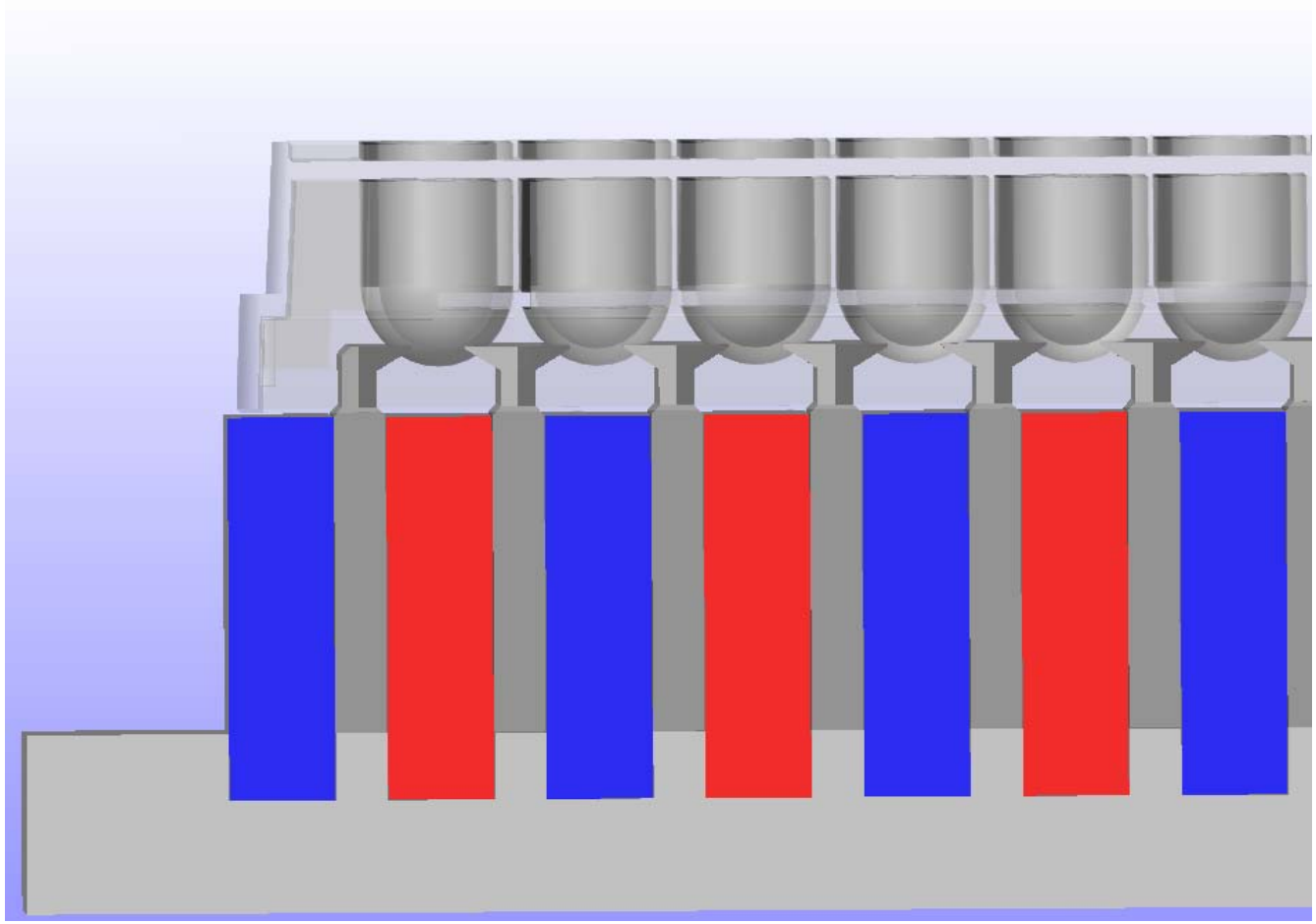
Microtiter Plate Well to Pole Relationship



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Continuing and Future Work

- Continued development of the hybrid concept for higher performance and broader applicability
- Fabrication of new, long period device for 1 and 2 ml deep well plates
- Hybrid variants for single molecule manipulation under rapid development
- Bio-medical applications of Hybrid technology in conceptual stages

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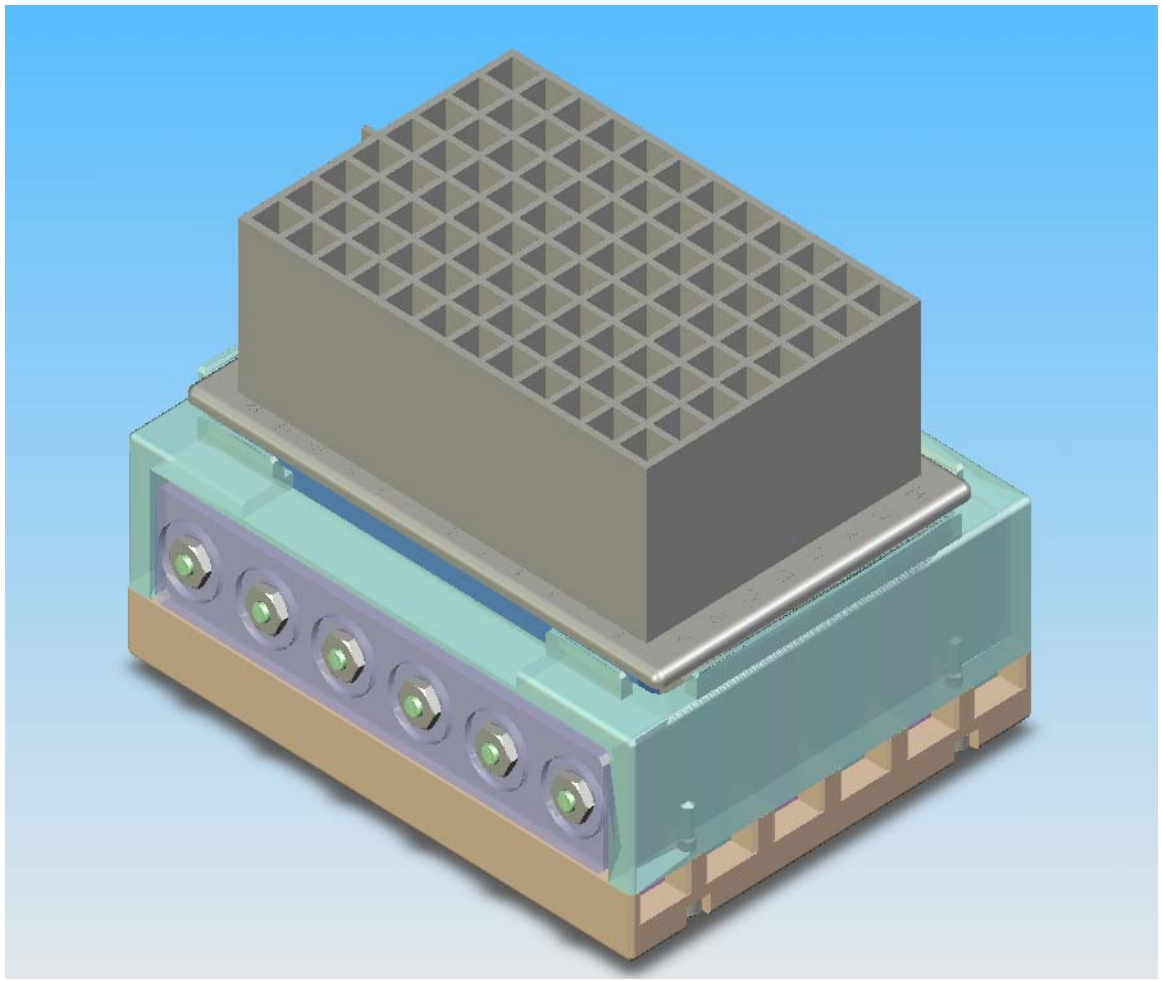
Long Period Hybrid w/ 2 ml Deep Well Plate



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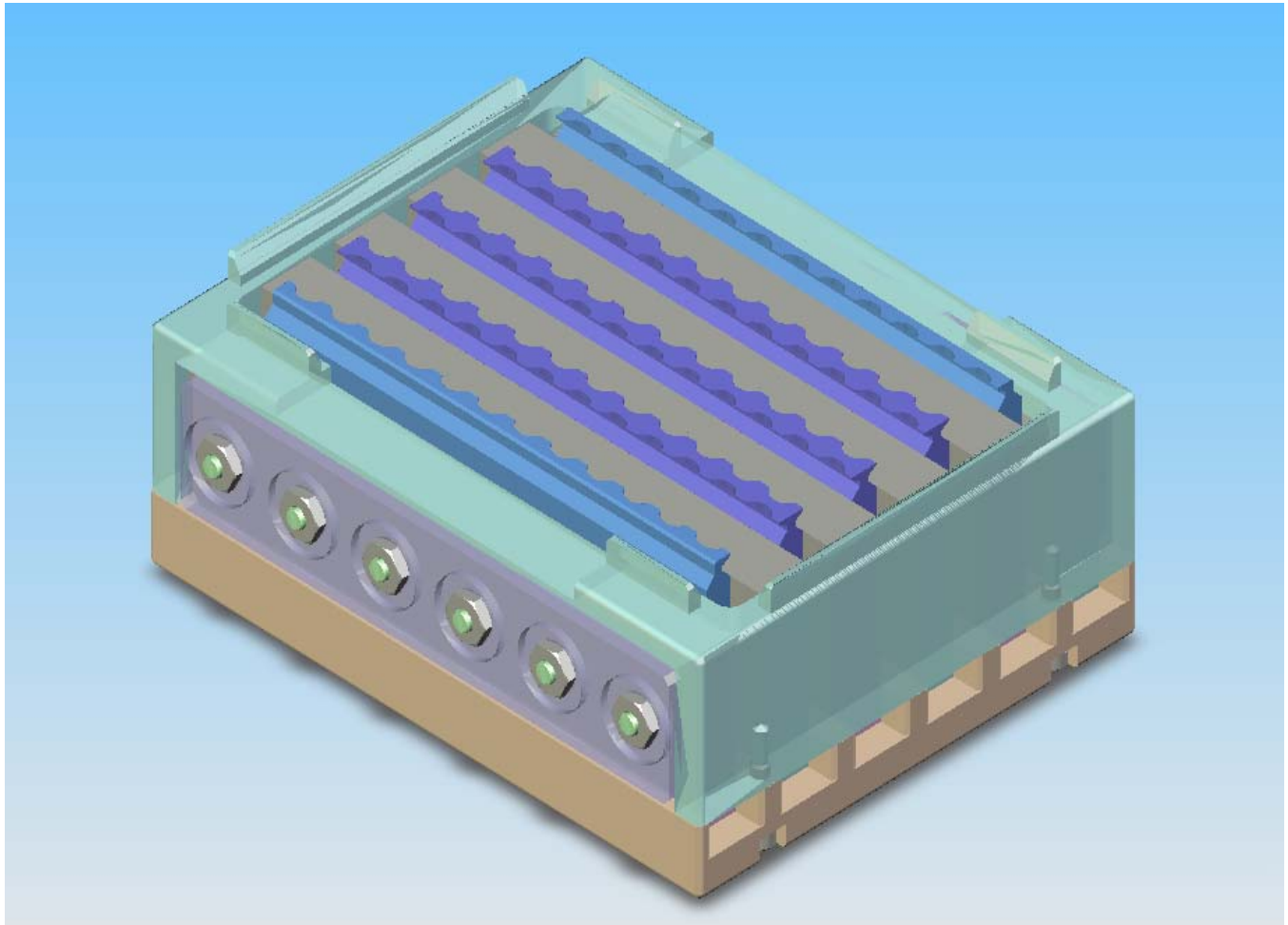
Long Period Hybrid w/ Upper Interface



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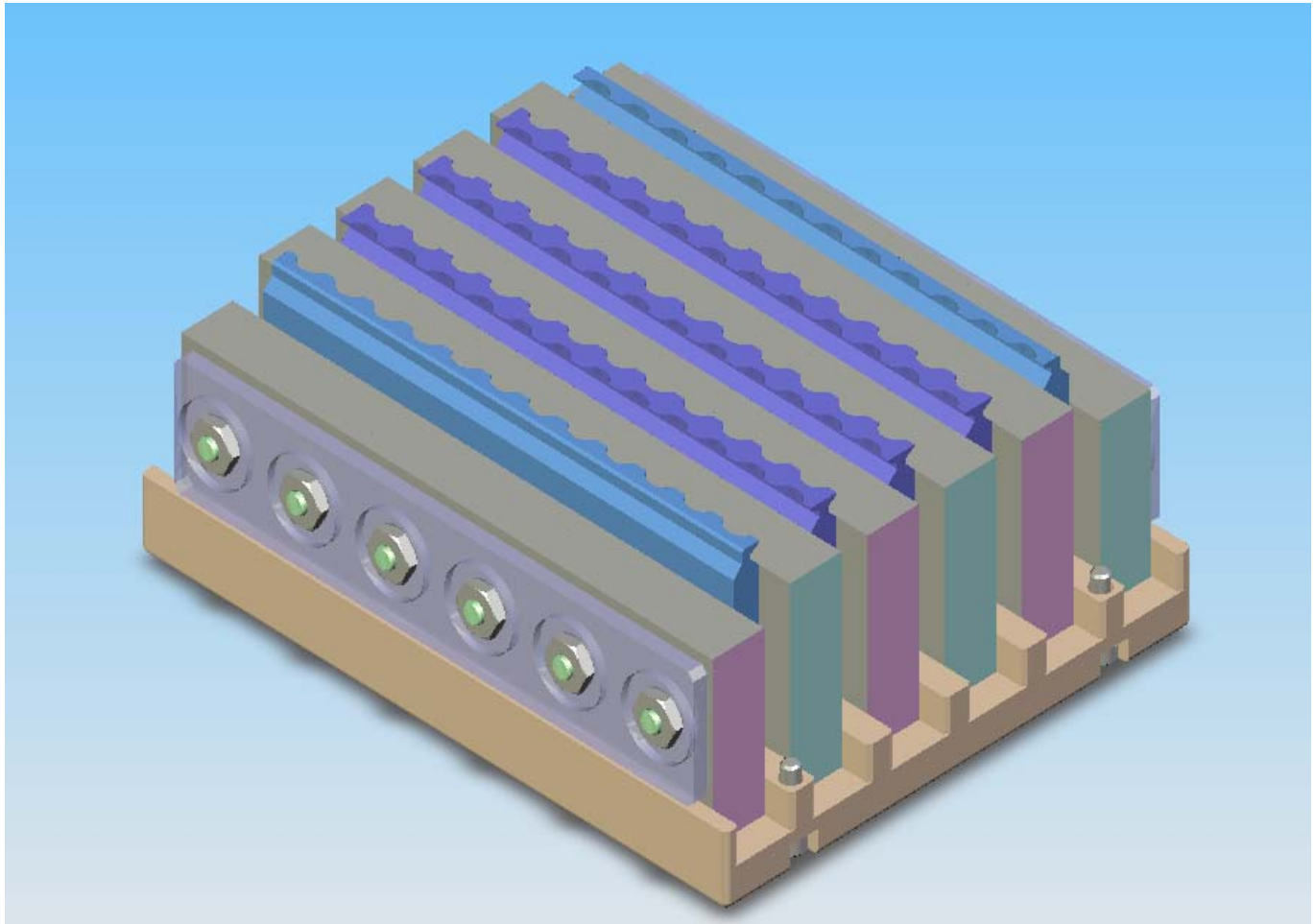
Long Period Hybrid w/o Upper Interface



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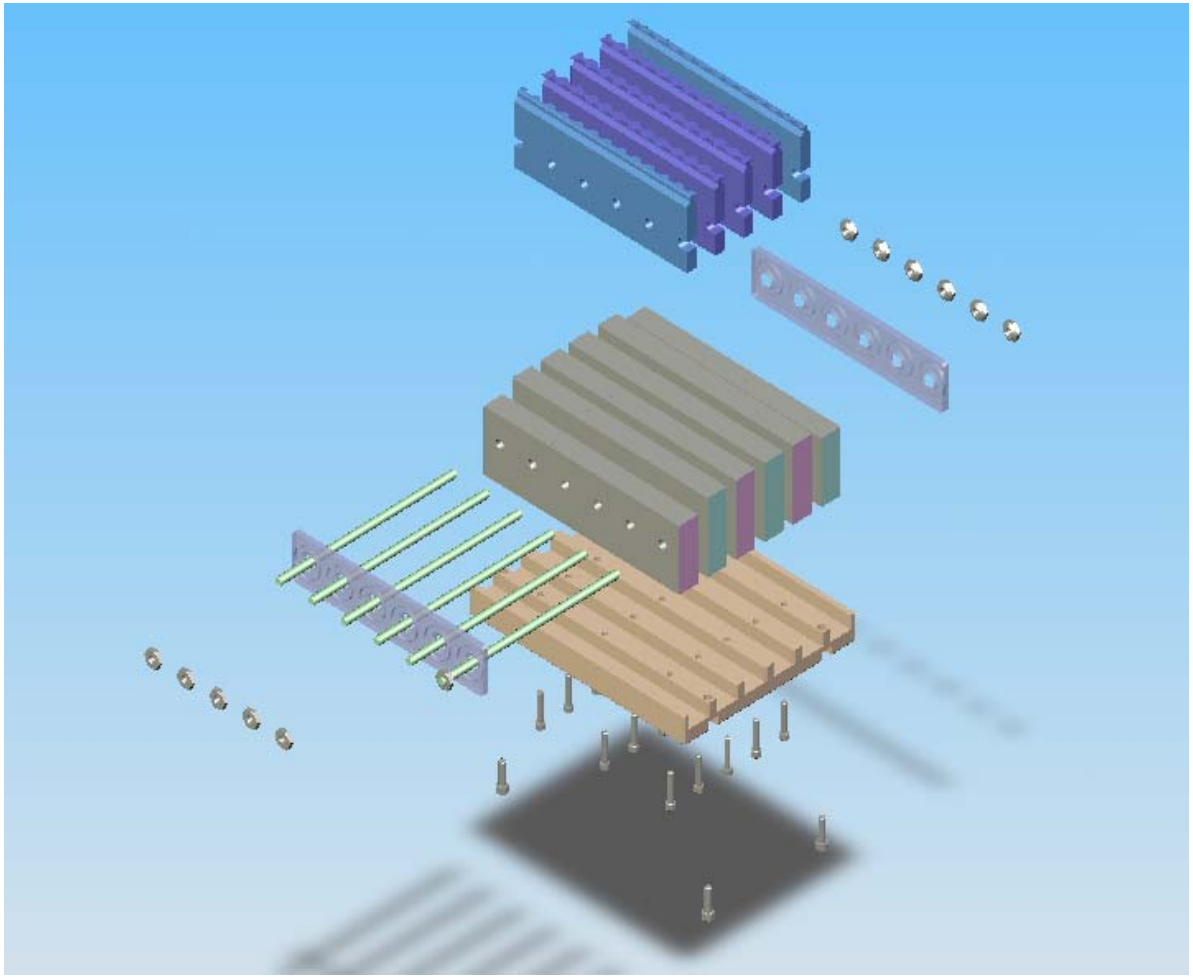
Long Period Hybrid – Exploded View



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Technology Transfer Opportunities

- Hybrid magnetic technology being patented by the University of California and Lawrence Berkeley National Laboratory
- Hybrid technology available for transfer to industry through the Tech Transfer Department of LBNL
- LBNL evolving as a center for advanced magnetic R&D for genomic, proteomic and bio-medical applications
- LBNL open to collaborative development efforts as part of its tech transfer process

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Advanced Fabrication Facilities at Lawrence Berkeley National Laboratory

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State-of-the-Art High Precision Machine Tools

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