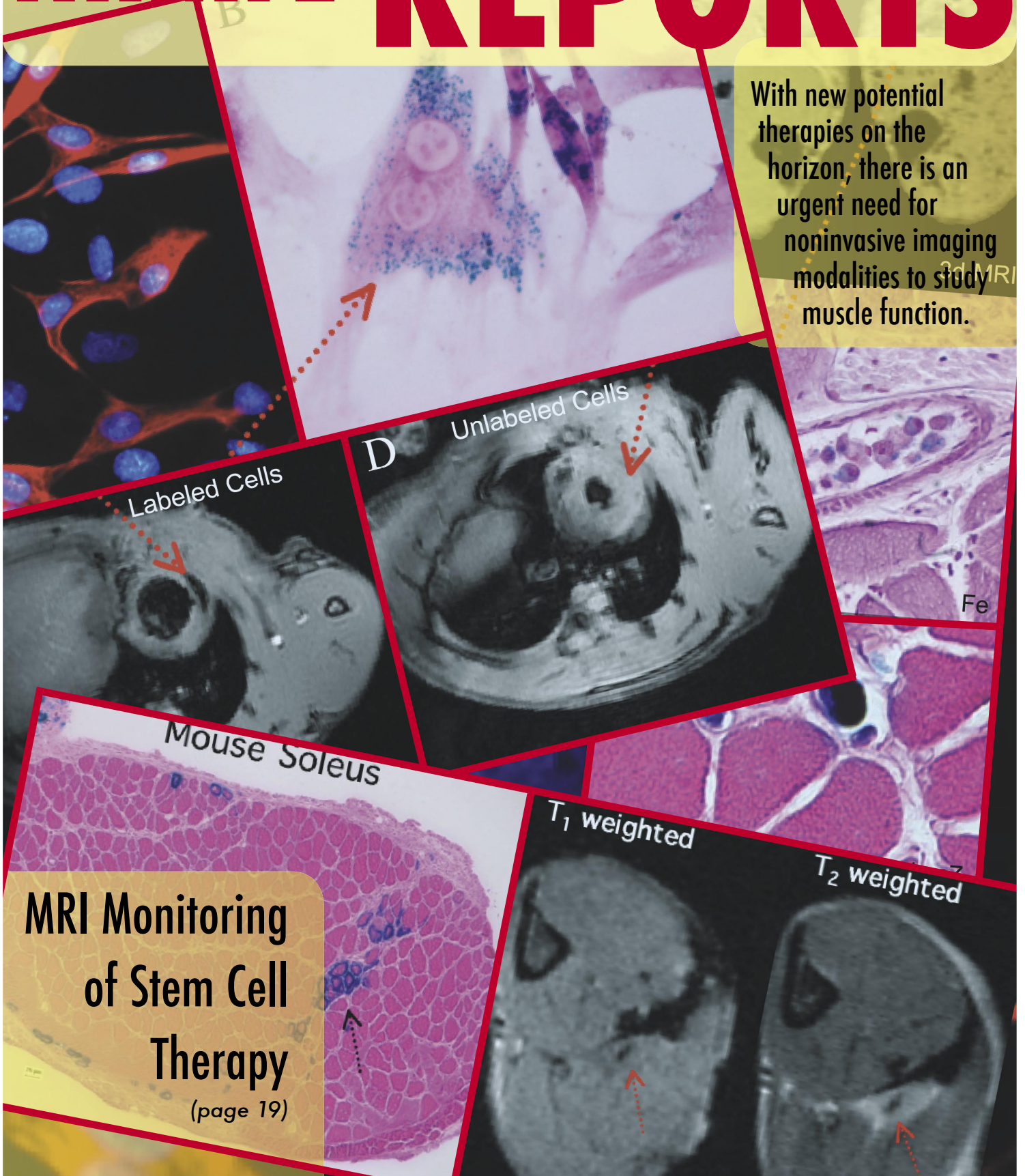


NHMFEL REPORTS

With new potential therapies on the horizon, there is an urgent need for noninvasive imaging modalities to study muscle function.



MRI Monitoring of Stem Cell Therapy

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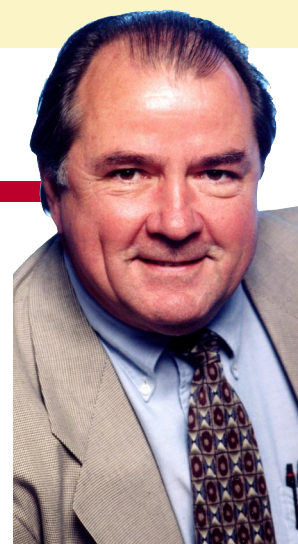
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FROM THE DIRECTOR'S DESK

Envisioning Science in High Magnetic Fields —the Next Decade & Beyond

NHMFL Renewal Activities Underway

The National Science Foundation's current 5-year award for the NHMFL extends through December 2005. During this period, the laboratory has already seen significant growth in interdisciplinary research activities, developed new probes and instrumentation that open new science opportunities, and advanced the state-of-the-art of resistive, pulsed, and superconducting magnet technology. In concert with these efforts, our educational programs—REU, RET, tours, open house, outreach—have continued to grow and be enhanced, and new partnerships are extending the laboratory connections among students, teachers, and scientists (see Dr. Dixon's article on page 14).



Jack E. Crow

Are we satisfied? Are we secure? No, and no. While the laboratory is extremely pleased and proud of its accomplishments, our view is *always* focused on the future. What's next? How can we make it better? What will this achievement enable? The new world-record 5 T high temperature superconducting magnet insert is a good example (see Dr. Schwartz's article on page 15). The successful test of this magnet is the culmination of a three-year university/industry partnership, and the project leader for Oxford Instruments, Dr. Ken Marken, summarized the effort *and the expectations* nicely: "The drive for ever higher fields in commercial NMR spectroscopy magnets was a compelling motivation for Oxford's investment in this achievement, and we look forward to using the technological advances demonstrated in our high field business."

Just as Oxford Instruments is looking ahead, so are we. The NHMFL renewal proposal will be submitted to NSF in December 2004, and activities focused on re-evaluating our vision and goals are already underway. While the proposal will specifically address 2006-2010, our focus and planning are on opportunities in high magnetic field science—and the development of new facilities in support of these opportunities—for the next 10 to 15 years. Drafting the proposal is a process that includes many activities. For example, the Users' Committee will meet on November 14-15 at Los Alamos, and the first day will be a workshop on the most promising topics in condensed matter science. The Users' Committee Chair Roy Goodrich has also posted a confidential Users Survey on the Louisiana State University Web site (www.phys.lsu.edu/nhmfl) and is aggressively seeking input about the operations, facilities and techniques, and scientific initiatives impacting the future of the NHMFL.

NHMFL faculty, along with external collaborators and users, are also developing white papers on topics such as nano-probes and thermal dynamic probes, spintronics, organics, NMR in pulsed magnet fields, and other areas of great interest and potential. A Renewal Retreat will be held in January where these papers will be presented and discussed.

Several conferences in 2004—including APS (March 22-26), the 16th International Conference on High Magnetic Fields in Semiconductor Physics (August 2-6 in Tallahassee), the Applied Superconductivity Conference (October 4-8 in Jacksonville), the 10th Anniversary NHMFL Celebration (October in Tallahassee), the 15th Conference of the International Society of Magnetic Resonance (October 24-29, Jacksonville area)—will provide additional opportunities to meet with and listen to both current and potential users. Special forums are being planned in association with several of these events.

In addition to addressing exciting science opportunities and the development of supporting facilities, the laboratory is very hopeful that the proposal to NSF will include a renewed commitment by the State of Florida. The leadership of Florida State University and the University of Florida are jointly requesting supplemental funding from the Florida Legislature that convenes in the spring. This request, which is reflective of the unique state-federal partnership that has underpinned the laboratory's successes, is focused at upgrading the

laboratory's infrastructure, such as power supplies and cooling systems and providing new research space to support the expansion of the user programs to new areas. The State assistance will ensure that the laboratory maintains its worldwide leadership in research facilities for high magnetic fields. This supplemental support follows on new State and NSF investments being made this year to develop a dedicated optic user facility incorporating a 20 T superconducting magnet, a split resistive magnet, and a clean room to house new time-resolved optics capabilities.

As I remarked in this space in the last issue, I cannot recall a time when the laboratory was surrounded by so much genuine interest, support, and leadership. This feeling continues, and is buoyed by the recent NSF External Site Review held in October. While the official Review Report has not yet been received, it appears that it will be a very positive review of the current program and prospects for the future. The momentum continues to build here at the NHMFL, and we are energized by the challenges and opportunities.

If *you* have ideas or suggestions for the renewal and the future of the laboratory, please feel free to contact me or any of the facility directors directly. Your views are extremely important to us.

Best regards,

Jack Crow

Correction: We regret two mistakes that appeared in this column in the last issue of *NHMFL Reports* in the discussion of the External Advisory Committee. The correct affiliation for Alexis Malozemoff is American Superconductor Corp. We also apologize to Ronald Scanlan for misspelling his name.

FROM THE CHIEF SCIENTIST'S DESK

J. Robert Schrieffer



The current status of Magnetic Materials Science and Engineering at the NHMFL is discussed in relation to future developments in these areas. NHMFL Chief Technology Officer Hans Schneider-Muntau discusses various opportunities for new projects.

Materials Research for Advanced Magnets

H.J. Schneider-Muntau, NHMFL

K. Han, NHMFL

The world records achieved at the NHMFL—the 25 T high-temperature superconductor (HTS) insert, the 33 T resistive magnets, and the 45 T hybrid magnet—are the result of a visionary magnet science and technology program from the beginning and continuous development work over many years. The 25 HTS insert is the consequence of many years' efforts, and a fruitful and trustful cooperation with industry. The success of the resistive and Hybrid magnet program would not have been possible without the invention of the Florida-Bitter magnet by one of the authors. The achievements with our pulse magnets put us on equal footing with other laboratories. The 900 MHz system will be the largest high-field magnet ever built. These accomplishments conclude the build-up phase as suggested by the Seitz-Richardson report.

It is a relevant question to ask what should be the next step. A common feature of all our magnets is that, after having developed a detailed understanding of the physics of magnets, and consequently optimized magnet design, we find our limitations in the deficiencies of the materials we have to use. If we want to maintain our leadership, we now have to break new grounds in materials research for magnets. Better conductors, insulators and reinforcement materials would not only help to achieve higher fields but would also improve the quality of the magnets, such as higher longevity, and better efficiency. In the following, we propose material development activities that are crucial for further progress in magnetic fields. We will deal with the major constraints in HTS, resistive, and pulse magnets through the limitations imposed by the mechanical properties of the conductors and reinforcement materials. We then propose a variety of approaches to establish a tailored materials development program.

Material Limitations in High-Field Magnet Designs

High-Temperature Superconductor Magnets

During the development of the 5 T HTS insert, major design challenges had to be overcome, such as space limitation because of the inner diameter of the outer magnet, high Lorentz forces due to the background field, magnetic interaction between the two coils, the anisotropy of the conductor, and other issues.¹ The step to higher fields with HTS inserts will need better conductors and reinforcement. Similar to Nb_3Sn , HTS conductors have a critical strain value beyond which strain degradation occurs. For most of the alloy-clad Ag conductors a strain tolerance of 0.4 to 0.5% has been demonstrated. The strain on the conductor can be reduced by adding reinforcement that shares part of the Lorentz forces. The Young's modulus of the reinforcement determines the load distribution between the conductor and the reinforcement. The presence of the reinforcement dilutes the current density of the winding, and a reduced average overall current density results, limiting the achievable field. Figure 1 shows that an increase of the current density within the superconductor only translates into a modest increase in average current density of the reinforced conductor, and levels off for higher current densities.

It results that future efforts have to focus on conductors with higher strain tolerance, and better reinforcement materials. Multiphase alloys, such as MP35N, with an ultimate tensile strength (UTS) of 2.5 GPa and a Young's modulus of 240 MPa at 77 K,³ or composites of organic fibers, such as Zylon, with a UTS of up to 5 GPa and Young's modulus of 180 GPa,⁴ might be materials of choice for the generation of even higher fields with HTS. Organic fibers have the additional advantage of being good insulators and not magnetic. Differences in thermal contraction between conductor and reinforcement would have to be investigated. The method developed at the NHMFL to coat the reinforcement tape

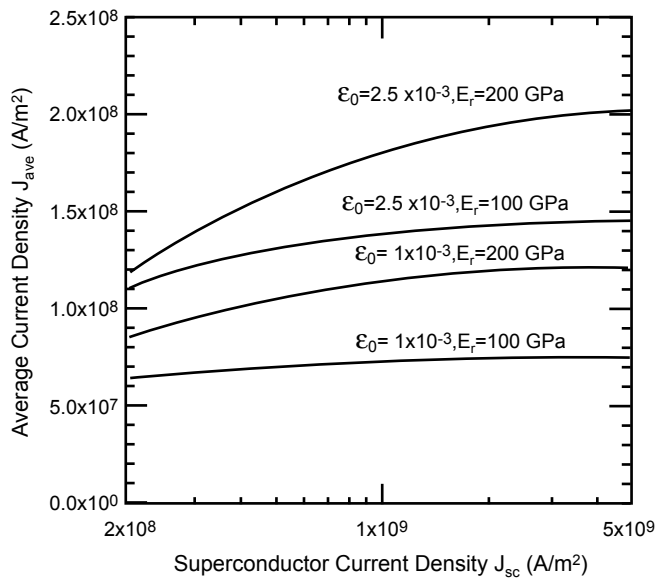


Figure 1. The average current density of the reinforced conductor as a function of the current density in the superconductor. Parameters are the allowable strain of the conductor, 0.1% and 0.25%, and the modulus of the reinforcement, after reference 2.

with ceramic insulation is very promising,⁵ and could be applied to MP35N. It remains, however, the general need for conductors with higher strain tolerance, and especially for high-strength, high-modulus reinforcement material, which can be co-wound or integrated in the conductor.

Resistive Magnets

There are three important parameters, that determine the strength of the magnetic field that can be achieved: the available power, the degree of optimization of the magnet design, and the materials used. The interaction between these three parameters is such that extra power can compensate for a bad design or insufficient materials. Considerable efforts have gone into the understanding of the physics of magnets, with the result that the NHMFL has not only the most efficient but also the most cost-effective, high-power magnets in the world. This was made possible through the invention of the Florida-Bitter magnet.⁶ Future improvements will have to focus on increasing the reliability even further and introducing the right measures to cope with the endforces.⁷

A basic relationship describing the power W required to generate a magnetic field B is $B=G(\lambda W/\rho a l)^{1/2}$ with λ the space or filling factor (conductor volume/total coil volume), ρ the specific conductor resistivity, $a l$ the inner magnet radius, and G the Fabry factor that includes coil shapes, dimensions, and current density distributions within the magnet. Because of the Lorentz forces, materials with higher strength have to be used if stronger fields are to be generated. If we have to choose a material with, let's say,

20% higher resistivity, an equal amount of additional power is needed if the same field is to be generated. Only high-strength conductors with higher conductivity than presently available can reduce this penalty, and should be part of a materials development program. Microcomposite conductors are most promising, since they have a significantly higher strength than the rule of mixtures predicts. It has been proposed to develop poly-helix magnets by machining thick cylinders with EDM and applying the Florida-Bitter pattern.⁸ To make this idea successful, it would require replacing the traditional method of swaging by new ways of cold working. Equal cross-section angular extrusion of CuAg microcomposites has been investigated earlier at the NHMFL.⁹ It remains the challenge to find a method for large cross-sections as required for poly-helix magnets, i.e., about 100 mm diameter. Another possibility exists in sandwiching the Bitter plates with thin plates of very-high-strength disks. This method would have the advantage that one could tailor turn by turn the conductor to the local stress level, and would be especially helpful in the end turns where high stiffness is required to cope with the endforces. Finally, one could also investigate in a jointing technique of the Florida-Bitter disks. In any case, the efficiency and field levels of resistive magnets can only be further improved when high-strength conductors with high conductivity in sheet form will be available.

Pulse Magnets

Four main parameters determine the field that can be achieved: the available energy, stored in a capacitor bank or a generator, the degree of optimization of the magnet design, the available materials, and the energy that can be dissipated in the magnet, i.e., its heat capacity. Similar to resistive magnets, limitations in materials or in the magnet design can be compensated by use of additional energy, however, with the penalty of increased magnet volume. Based on the analysis of resistive magnets, especially the poly-helix magnet, a detailed understanding of the physics of pulsed magnets has been developed, resulting in powerful computer codes to optimize the complex interactions of the many parameters.¹⁰ Radial stress transmission between the inner layers is suppressed for reduced hoop stress, and each layer has its own reinforcement. The Lorentz force is shared between the conductor and the reinforcement in an optimized way, i.e., the Young's moduli, strain tolerance, and strength of both are matched while maintaining the plastic deformation of the conductor within its allowable limits. Similar to HTS, higher fields could be reached if strength and Young's modulus of the reinforcement would be better, and if strain tolerance and fatigue behavior of the conductor could be improved. Corresponding requirements for the materials development are essential. In addition, conductors

with high conductivity and high heat capacity are needed for less heating. Generator-driven magnets require, because of their low operating voltage, conductors with large cross-sections, which are challenging to manufacture.

Materials Research

In the following, we list a variety of approaches to meet the above listed requirements for improved or new materials. The proposed methods represent a selection, which we consider promising.

Conductors

In *metal-metal microcomposites*, such as Cu-Ag and Cu-Nb, a strength level of up to 1.5 and 2 GPa, respectively, has been achieved in wires of small cross-section and is attributed to the refined structures, which can be achieved through specific manufacturing techniques. Figure 2 gives an example. Further optimization of the properties of these composites is possible. Particularly, to achieve the required high-strain tolerance, one can utilize heat treatment and changes in composition to modify the microstructure. For instance, by increasing the Ag content in Cu-Ag materials, low modulus conductors with the same strength could be produced, which translates into higher strain tolerance. Ultra-high ductility was reported in Cu by special heat treatment promoting microstructured components embedded in nanostructured components,¹¹ and we propose to apply the same method to CuAg microcomposites. Further systematic research should concentrate on interface structures, internal stresses, strain hardening, and thermodynamic properties of Cu-Ag and Cu-Nb composites. The interface structure, on both microstructural and atomic scale, governs the strengthening mechanism and physical properties (such as conductivity) of the composite. The internal stresses affect the elastic-plastic response of the conductors to Lorentz forces and thermal stresses.¹² After cold work, the two phases are exposed to induced stresses of opposite sign. We have shown that cyclic loading, for instance by operation in a pulse magnet, creates additional dislocations, which relieve the internal stresses resulting in a higher elastic stress range. This is related to the strain-hardening rate where basic research has the promise to develop conductors with higher strength and/or higher strain tolerance.

The development of *high-strength pure copper* through generation of nanograins and twins in addition to high-density dislocations seems to be very promising. The materials can be fabricated by cryogenic deformation plus thermal heat treatment, which have shown to promote twin formations. Since twins strengthen the material significantly and have limited scattering effects on the electrons, it will provide high strength and high conductivity to the conductors. Other approaches we can consider are to promote the twin

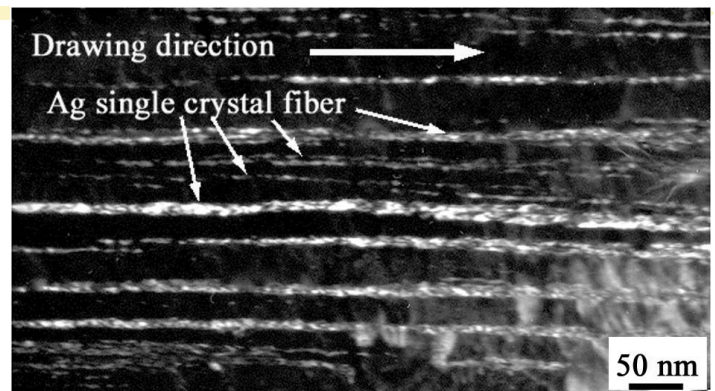


Figure 2. Dark field transmission electron microscopy image showing single nano-Ag fibers embedded in Cu matrix in a Cu-Ag microcomposite high-strength conductor. The contrast within a crystal of nano-Ag fiber indicates the high internal stresses in the fiber.

formation using electro-deposition or similar methods, such as physical vapor deposition. It has been reported that these techniques can produce a high density of twins in Cu, which strengthens it significantly. The work performed at the NHMFL, and funded through an In-House Research Program award, has shown that cold work at cryogenic temperatures is a very promising method to form high-density dislocations and nanotwins.¹³ We have obtained a UTS of 580 MPa for pure Cu at room temperature and 680 MPa at 77 K with a conductivity of 96% of the international annealed copper standard. These values were obtained with an area reduction of only 90%. A necessary second step is now to improve the annealing behavior by investigating low-alloyed Cu or low weight-percent CuX microcomposites, where X is a second component with little impact on the Cu conductivity.

Macrocomposites, and especially hybrid-composites consisting of high conductivity materials, such as Cu, Cu alloys or microcomposites, and high strength reinforcement materials should be assessed. Future research should consider the use of different reinforcement components, such as maraging steels, that are strengthened mainly by the precipitation of an intermetallic compound rather than deformation. One should investigate different conductor geometries and the bonding issue, either by cold rolling or adhesives. First studies have shown that hybrid-composite conductors, made from a mixture of microcomposite conductors, high-strength Cu wires, and high-strength reinforcement strips would be a very promising way to tailor conductors to specific applications.¹⁴ Instead of using stainless steel for cladding the Cu or Cu composite core, we will consider the repetitive roll bonding to combine Cu with reinforcement material. In order to achieve strength of greater than 1 GPa with 30% volume fraction of the reinforcement material, as it is required for reasonable conductivity, the strength of the reinforcement materials must be around 3 GPa.

Reinforcement Materials

Various *ultra-high strength and high-modulus superalloys*, such as cobalt alloys have high modulus and high strength. At the NHMFL, we have obtained a UTS of 2.6 GPa at 77 K in MP35N, which has a modulus of 240 GPa at 77 K. Our investigations show that texture and nanoplatelets development during the cold work contribute to the strength and anisotropy of the cobalt alloys. With the goal of obtaining reinforcement material of up to 3 GPa, we propose to optimize the texture and refine further the structure. Of extreme importance is to investigate the addition of high-modulus elements to the existing alloys in order to achieve even higher-modulus alloys. We also propose to study and optimize the thermal expansion coefficient to match favorably conductor and reinforcement for magnets operated at cryogenic temperatures.

Metallic glass, formed by supercooling the liquid state of metallic alloys, was reported to have very high fracture strength (5.2 GPa) and modulus (270 GPa).¹⁵ The mixture of glass and nanocrystalline can produce high-strength materials with acceptable ductility. Up to now, little work has been done for cryogenic applications of this material, but may be promising.

High-strength epoxy-matrix composites have a great potential for further improvements. Recently, bone-shape Ni fibers were found to strengthen cement significantly. It is suggested to develop high-strength M5 or Zylon fibers with bone shape to strengthen the matrix. We also suggest developing composites with different architectures from these strong fibers so that the composite has the strength in the direction optimized for magnet design. The bonding between the fibers and the epoxy would have to be investigated, both experimentally and with simulation approaches, such as molecular dynamics.

Conclusions

The detailed understandings of the physics of magnets, and consequently magnet analysis, have obtained a high degree of perfection over the years, resulting in powerful optimization codes and international leadership in high-field magnet technology. The world records underline these successful efforts. Further progress now depends crucially on the availability of better materials for magnets.

Based on our exploratory work during the last years on conductors, we propose to focus on micro- and macrocomposite conductors, and high-strength Cu. The potential of cryogenic deformation and tailored macrocomposites is only in its beginnings and should be further explored.

Concerning reinforcement materials, we encourage investment in the development of high-modulus metal alloys and organic fibers at the theoretical limit of ultimate strength. Such materials would excite enormous industrial interest.

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NEWS from the DC FIELD FACILITY

Angle-Resolved Mapping of the Fermi Velocity in a Quasi-Two-Dimensional Conductor

A. Kovalev, University of Florida, Physics
S. Hill, University of Florida, Physics and NHMFL

Microwave spectroscopy has been utilized as a means of studying the electrodynamic properties of metals for well over half a century, especially resonant absorption in an external DC magnetic field. Quasiparticles in such conductors usually move on closed periodic trajectories in reciprocal (k -) space, or cyclotron orbits in real space. When any period associated with this motion matches the period of the external electromagnetic field, so-called cyclotron resonance (CR) occurs if the condition $\omega_c \tau > 1$ is satisfied, where ω_c is the cyclotron frequency and τ is the relaxation time; ω_c depends on the magnetic field strength, and on the cyclotron mass (m_c)—a characteristic of the Fermi surface (FS).

In layered conductors, the FS may be either quasi-two-dimensional (Q2D), quasi-one-dimensional (Q1D), or a combination of both.¹ In the Q2D case, the FS is a warped cylinder with its axis perpendicular to the layers (see Figure 1) while, in the Q1D case, the FS consists of a pair of warped sheets at $\pm k_F$. Because of this reduced dimensionality (and reduced $v_F \sim 10^5$ m/s), several new effects in the microwave conductivity have been reported, one of which is the observation of multiple periodic orbit resonances (POR) in Q1D systems.² In this report, we detail a new magnetic resonance phenomenon that enables angle-resolved mapping of the in-plane Fermi velocity for a Q2D conductor.³ As such, this technique is complementary to Angle-Resolved Photo-Electron Spectroscopy (ARPES⁴), i.e., it can provide information concerning the in-plane momentum dependence of the density-of-states ($\propto v_F$) and quasiparticle scattering rate (τ^{-1}). We illustrate the utility of this method for the κ -(BEDT-TTF)₂I₃ (BEDT-TTF=bis-ethylenedithio-tetrathiafulvalene) organic superconductor, which has a relatively simple and well characterized FS (see Figure 1).¹ This technique, however, could equally be applied to more exotic Q2D conductors (e.g. Sr₂RuO₄). As many ARPES investigations have shown, angle-resolved FS spectroscopies have the potential to reveal critical information concerning the various instabilities that give rise to unusual magnetic and superconducting states in low-dimensional correlated electron systems.⁴

High-field measurements (up to 33 T) in the conventional geometry (field \perp layers) performed at Tallahassee reveal a form of closed orbit POR. The new open orbit effect appears when one aligns the magnetic field within the layers.³ In this case, the quasiparticle motion is *principally* open and periodic (except for a small fraction of the total electrons—see Figure 1a); this is due to the underlying periodicity of the crystal which leads to the FS warping. The period depends on the magnetic field strength, B , and on the velocity component (v_{\perp}) perpendicular to the field. Averaging over the FS leads to the result that the extremal perpendicular velocity (v_{\perp}^{ext}) dominates the electrodynamic response, giving rise to a resonance in the interlayer conductivity (σ_{zz}) when the period of the electromagnetic field matches the periodicity of the extremal quasiparticle trajectories, i.e., when $\omega = \omega_c^{ext} (\equiv eBa v_{\perp}^{ext}/\hbar, a$ is the interlayer spacing). Measurement of ω_c^{ext} , as a function of the field orientation ψ within the xy -plane, yields a polar plot of $v_{\perp}^{ext}(\psi)$. The procedure for mapping $v_F(\phi)$ is then identical to that of reconstructing the FS of a Q2D conductor from the measured periods of Yamaji oscillations.¹ Analytically, assuming one can measure $v_{\perp}^{ext}(\psi)$, it is possible to generate the Fermi velocity $v_F(\phi)$ using the following transformations (see also Figure 1b):

$$v_F = \sqrt{(v_{\perp}^{ext})^2 + v_{\parallel}^2}; \quad \phi = \psi + \arctan\left(\frac{v_{\perp}^{ext}}{v_{\parallel}}\right); \quad v_{\parallel} = -\frac{dv_{\perp}^{ext}}{d\psi} \quad (1)$$

A small platelet shaped (0.7×0.4×0.12 mm³) single crystal of κ -(BEDT-TTF)₂I₃ was studied using a phase sensitive cavity perturbation technique described elsewhere.⁵ The FS of κ -(BEDT-TTF)₂I₃ may be calculated using a 2D tight binding model, resulting in a network of overlapping Fermi cylinders,¹ as shown in Figure 1c. All measurements were carried out at 4.5 K, above the superconducting transition temperature ($T_c = 3.5$ K), and at a frequency of 53.9 GHz.

In Figure 2, we plot the experimentally determined $v_{\perp}^{ext}(\psi)$ on a polar diagram. The dashed line is a fit to Equation 1, and the

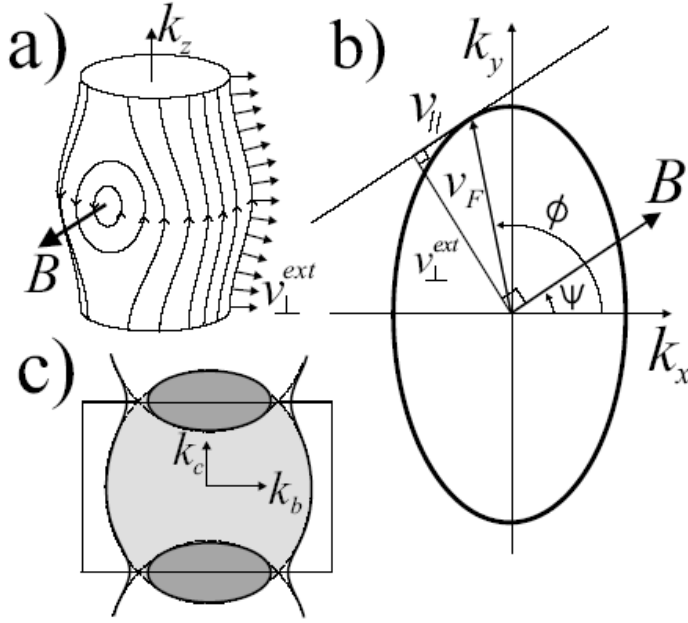


Figure 1. (a) An illustration of the quasiparticle trajectories on a warped Q2D FS cylinder for a field oriented perpendicular to the cylinder axis. The resulting trajectories lead to a weak modulation of the quasiparticle velocities parallel to k_z and, hence, to a resonance in σ_{zz} . (b) The thick line shows $v_F(\phi)$ according to Equation 1; the right angle triangle illustrates the relationship between $v_{\perp}^{ext}(\psi)$ and $v_F(\phi)$. (c) The Fermi surface of κ -(BEDT-TTF) $_2$ I $_3$.¹

solid line is the corresponding Fermi velocity; the extremal values are $v_{xm} = 1.3 \times 10^5$ m/s and $v_{ym} = 0.62 \times 10^5$ m/s. This anisotropy is in good agreement with the known anisotropy of the small Q2D FS for κ -(BEDT-TTF) $_2$ I $_3$ (dark shaded region in Figure 1c). If one assumes a parabolic dispersion, it is possible to compare our data with the band parameters determined for the large Q2D β -orbit from optical data by Tamura *et al.*⁶ In particular, we may estimate the effective mass along the c -direction as $m_{c\beta} = 2.5 m_e$, which compares to the value of $2.4 m_e$ determined from the optical measurements.⁶ Based on the known value for the area of the small Q2D section of the FS (α) in k -space, we may estimate the momentum averaged cyclotron mass to be $m_{c\alpha} = 1.7 m_e$, while the experimental value deduced from the SdH and dHvA effects is $\sim 1.9 m_e$.⁷ Thus, our findings appear to be in excellent agreement with published data.

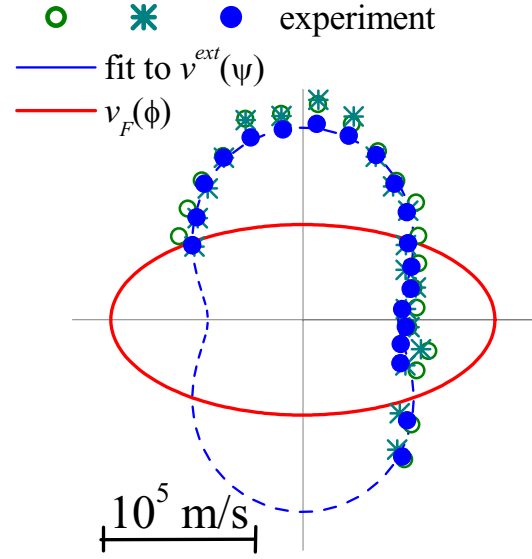


Figure 2. Polar plot of experimentally obtained $v_{\perp}^{ext}(\psi)$; the dotted line is a fit and the solid line is the resultant $v_F(\phi)$.

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NEWS FROM NMR USERS PROGRAM

The Role of the Turn Symmetry in the Folding and Stability of FGF-1

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The ability of proteins to fold up into a unique structure is the essence of the protein folding problem, and also is highly relevant to the area of self-assembling systems in the emerging nano-biotechnology field. In thermodynamic terms, protein folding and self-assembly is a delicate balance between enthalpy gain and entropic loss as an ensemble of conformational states accessible to a single polypeptide chain adopts a single (or severely limited number of) conformation(s). In kinetic terms, such structural changes must also occur within a time frame appropriate for living systems. In contributing to our understanding of the protein folding problem, the Logan and Blaber groups are collaborating on studies of hairpin turn regions within human acidic fibroblast growth factor (FGF-1). As outlined below, FGF is an interesting model system for protein folding studies. In addition, FGF is a potent growth factor (i.e. stimulator of cell growth). For example, FGF is known to stimulate angiogenesis (the growth of new blood vessels), and it is finding some clinical applications as a topical applied to cardiac muscle damaged by artery obstruction. It is hoped that the knowledge of FGF folding and structure coming from this research may increase its potency.

FGF is a small protein composed of primarily β -sheet and hairpin turn secondary structures (Figure 1). The FGF-1 structure is highly symmetric, with a three-fold symmetry axis being present down the barrel of the protein. This structural symmetry is not reflected in the amino acid sequence, as symmetry-related secondary structures and tertiary interactions are generated by different amino acid sequences. This raises some intriguing questions about how the symmetry of protein structure and sequence relates to the folding and stability. For example, why is the structural symmetry *not* reflected in sequence symmetry? It is possible that there is no evolutionary pressure to maintain the sequence symmetry and so there is drift in the amino acid sequence, e.g., replacing certain amino acids in the sequence does not significantly alter the stability, folding, or function of FGF-1, and so these residues would not be under evolutionary pressure to be retained. A more interesting question is whether there is evolutionary pressure to *reduce*

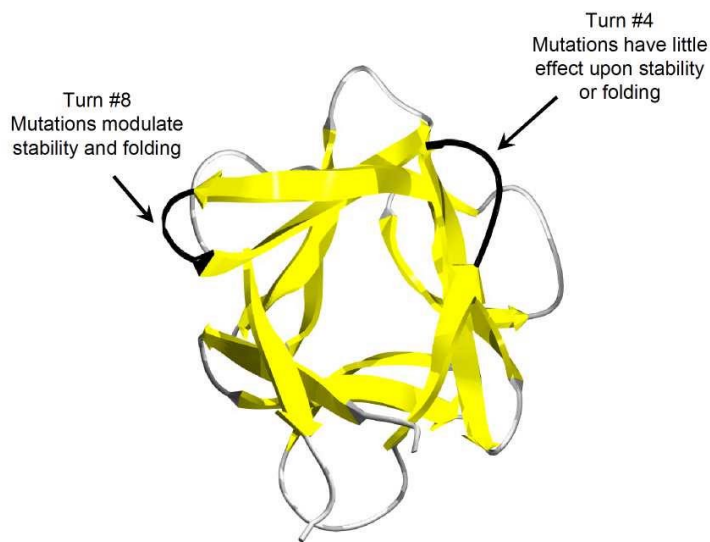


Figure 1. An illustration of the polypeptide chain conformation in FGF-1. Two turn regions are indicated in black shading: turns 4 and 8. Mutational studies indicate that changes in the amino acid sequence of turn 4 have little effect upon the stability or folding kinetics of the protein, while the amino acid sequence within the turn 8 region can have substantial effects.

the sequence symmetry. What would be the consequences for folding if the sequence were more symmetric? Would the protein fold to the same structure or would there be an increase in the percent of proteins that "misfold" by pairing incorrectly with the wrong β -strands?

Although α -helix and β -sheet secondary structures have been the subject of numerous biophysical studies, little is known regarding the thermodynamic and kinetic contribution to protein folding of hairpin turns. Turn regions are essential for the polypeptide to change direction and terminate the linear conformation of the other secondary structures. A key question to understand relates to the interplay between the energetics of the turn regions and the associated adjacent α -helical or β -sheet secondary structures. In other words, does the stability of the adjacent secondary structure drive the formation of the turn structure, or does the stability of the turn structure drive the formation of the adjacent secondary structure? The Logan and Blaber groups are investigating this question by mutating the amino acid sequence within specific turn regions in FGF-1 and determining the effects of such mutations upon the structure, thermodynamics and kinetics associated with the folding of the protein.

FGF-1 has 11 turns (12 if you consider the adjacent N- and C-termini as a discontinuous turn), and it is becoming clear that not all turns in FGF-1 are equivalent in their properties. Some turns appear to be merely connecting regions between highly stable adjacent secondary structures— substitution of the amino acids within these turns has essentially no effect upon stability, folding kinetics, or structure. In other cases, the turns appear to contribute substantially to either the stability or kinetics, and require a very specific amino acid sequence. Among these turns, turn 4 (connecting β -strands 4 and 5) and turn 8 (connecting β -strands 8 and 9) are related by three-fold symmetry of FGF. Turn 8 (residues E90-E91-N92-H93) is a type-I turn. Turn 4 (residues A49-E50-S51-V52-G53) is symmetry-related to turn 8 but forms a type II turn.

We wanted to determine why these two regions adopt different conformations, and to investigate the consequences of sequence and structure symmetry relationships between these turns. Therefore, a series of single-site mutations were designed to probe the thermodynamic importance of specific interactions that differ between these two turn regions, and also to systematically convert turn 4 into turn 8 sequence and vice versa.

Polyglycine Substitutions. Our first study systematically changed each residue in the turns 4 and 8 to the amino acid glycine. Glycine is an unusual amino acid in that it does not contain a "sidechain" group and so has fewer restrictions in the conformations that it can adopt compared to the other 19 amino acids. As shown in Table 1, substituting individual turn 4 residues into glycine did not significantly alter the thermodynamic stability or folding kinetics. Indeed, the E49G/S50G/V51G polyglycine mutant showed essentially the same stability and folding rates as wildtype. In contrast, changing His92 to Gly in turn 8 resulted in a substantial increase in stability of nearly 9 kJ/mol, due almost entirely to a 15-fold enhancement in the folding rate. Converting the remaining turn 8 residues into Gly yielded a mutant that had essentially the native state stability and folding. The dramatic effect observed in the H93G mutant reflects the steric interactions that arise from the large His sidechain at this

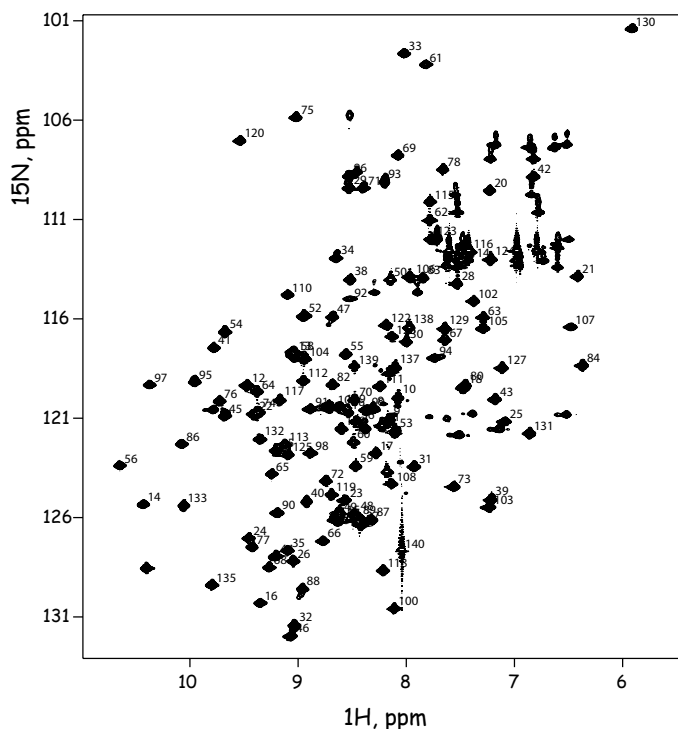


Figure 2. Two dimensional ^1H , ^{15}N single-quantum correlation spectrum of wildtype FGF indicating the assignments of the backbone amide resonances.

position. Removing this sidechain by glycine replacement facilitates folding by reducing steric interactions and strain, resulting in substantial structural stabilization. Why does nature retain this His residue at this position? Functional studies reveal that this His residue is required for activity, forming electrostatic interactions with negative residues in the receptor. Thus, the stability of the protein is sacrificed for biological activity. Indeed, structural studies have shown that receptor binding is accompanied by a conformational change in turn 8; perhaps the strain introduced by the His residue "cocks the trigger" providing additional driving force for binding.

Substituting Turn 8 into Turn 4 Sequence. The polyglycine data indicated that turn 4 was more "plastic" in that it readily accommodated amino acid substitutions. In contrast, turn 8 residues showed a higher requirement for the specific amino acid sequence. In the next study, we investigated the consequences of converting turn 8 into turn 4 by creating a triple-mutant, E91S/N92V/H93G (8 \rightarrow 4). The reverse mutant was also created, changing turn 4 into turn 8 (S50E/V51N/G52H; 4 \rightarrow 8). As shown in Table 1 there was little change in the stability of the 4 \rightarrow 8 mutant compared to the wildtype protein. As predicted from the polyglycine substitutions at this site, turn 4 is able to accommodate essentially any amino acid sequence at this position. The 8 \rightarrow 4 mutant was

Table 1. Stability of FGF-1 mutants.

Protein	$\Delta\Delta\text{G}$ (kJ/mol)
E49G/S50G/V51G	-1.6
H93G	-8.9
E91G/N92G/H93G	-1.5
S50E/V51N/G52H	1.9
E91S/N92V	6.5
E91S/N92V/H93G	2.1

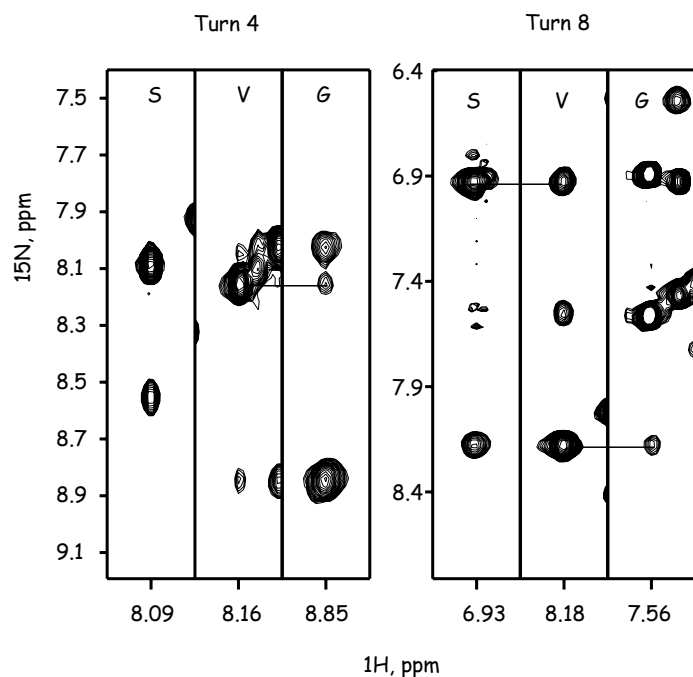


Figure 3. Composite plot of several slices taken from a 3D ^{15}N -separated NOESY-HSQC spectrum of the 8→4 mutant. The left panel shows the HN-HN NOEs observed for residues S50-V51-G52 of turn 4; the right panel shows the HN-HN NOEs observed for the same amino acid sequence in turn 8 (residues S91-V92-G93). The lines indicate the location of sequential and medium range NOEs observed for each residue.

slightly more destabilized than the other mutant. However, the majority of the destabilization arose from the E91S/N92V substitution (6.5 kJ/mol destabilizing compared to -8.9 kJ/mol stabilization from the H93G mutant). The reasons for the destabilization in the double mutant are not clear and are currently under investigation. Nevertheless, these studies further demonstrate the thermodynamic difference between turn 4 and turn 8 in that the same sequence at two symmetry-related positions has substantially different thermodynamic consequences for stability.

A key component of these studies is the structural analysis of these mutants. We have determined a high resolution structure of wildtype FGF-1 using X-ray crystallography, but the study of turn regions (and mutations therein) introduces unique problems for X-ray structure determination. In particular, it is the surface turn regions that are most often involved in crystal contacts. It is not uncommon for mutations in such regions to perturb crystal contacts and preclude crystallization. However, it is essential to understand the structural consequences of such mutations upon the turn regions. In the course of studying these turn mutations, we were unable to obtain critical structural information of some mutants using X-ray crystallography, and turned to NMR to solve this problem.

The first step was to confirm resonance assignments in wildtype FGF, for which a series of triple resonance NMR experiments were collected. The resulting assignments are indicated in Figure 2 which is a 2D ^1H , ^{15}N single-quantum correlation experiment (HSQC). We then repeated these experiments to obtain assignments for the 8turn4 mutant (not shown). We used these assignments to characterize the turn conformation for residues in turns 4 and 8 wildtype and mutant FGF-1 proteins. Figure 3 shows that the NOE patterns obtained for the ESGV residues in turn 4 and turn 8 in the mutant protein are different. Specifically, we observe intense sequential and medium-range NOEs between the amide protons of turn 8 residues but not for the same amino acids in turn 4. These data also support the thermodynamic and kinetic investigations that point to some fundamental difference in the two turn regions. This finding confirms that the turn conformation is not merely dependent on the local amino acid sequence, but depends, in some as yet undefined manner, on the tertiary structure imposed by the folded state of the protein.

The results to date indicate the following:

1. Turn regions related by structural symmetry do not necessarily have equivalent thermodynamic and kinetic contributions towards protein stability and folding.
2. The alternative turn structures 4 and 8 in FGF-1 are not due to the local sequence within the turn, nor to structural differences in the adjoining secondary structure (i.e. anti-parallel β -strands). We are left with the conclusion that amino acid side chains, located outside of the turn region (and possibly within the adjoining secondary structure) are the prime determinants of the turn structures in turns 4 and 8.
3. Turn 8, and structural alterations within this turn, is essential for receptor binding. We conclude that the dynamics associated with this structural alteration upon receptor binding are associated with strain within this turn (at position 93 as determined by Gly mutagenesis). Again, this strain appears related to interactions with side chains outside the turn.

The focus for future work is related to elucidating which of the neighboring residues to the turn(s) are influencing structure and strain. Another area of study will be to understand the limitations upon turn identity for symmetry-related turns in structural superfolds.



EDUCATION at the NHMFL Partnerships in Learning

The Center for Integrating Research and Learning expands its reach through new and continued partnerships and collaborations. New directions in science research and emphasis on technology's response to a growing need for innovative sources of energy demand attention from the education community. Teachers, students, and scientists recognize the need to translate complex concepts in order to prepare the next generation of workers in a high-tech society. The Center has responded to this need by teaming up with other groups trying to address this need.

Our new "Superconductivity Package" is the result of two years collaboration among teachers, scientists, researchers, and administrators. Brian McClain and Kenneth Bowles, two teachers from the Research Experiences for Teachers program, worked for two consecutive summers with Justin Schwartz and Sastry Pamidi at the NHMFL to explore ways to translate superconductivity for teachers and students. Pat Dixon and Gina Hickey at the NHMFL developed activities and materials for teachers to conduct hands-on inquiry-based activities. Sue Butler and Jim Meen from the University of Houston, David Larbalestier, Mel Adams, and Matt Jewell from the University of Wisconsin, and Ysonde Jensen and Pat Dixon from the NHMFL worked to make the first interactive I-Wall display on superconductivity a reality. The I-Wall and superconductivity content for students, teachers, and the general public was showcased at the Florida Association of Science Teachers in Jacksonville, Florida, October 16-18, and garnered a great deal of attention. Sponsored by the National High Magnetic Field Laboratory, the Center for Advanced Power Supplies (CAPS), the University of Houston, the University of Wisconsin, IEEE, and the Applied Superconductivity Conference, Inc., a 12-foot interactive traveling museum exhibit is being developed and will be unveiled at the Applied Superconductivity Conference in Fall 2004 in Jacksonville, Florida.

The superconductivity package of activities addresses topics and concepts basic to our understanding of superconductivity: the First Law of Thermodynamics, resistance and electric current, magnetic field and magnetic flux, magnetism and electricity, superconductors versus

resistors, superconductivity as a field of study, and the history of superconductivity and recent developments. Teachers and students will be involved in the conference through a workshop designed to disseminate the materials, to provide training on how to use the materials and activities, and to preview the museum exhibit and a version of the exhibit suitable for classrooms. Another feature of the collaboration is an effort to provide strategies for scientists who wish to conduct science outreach.



Building on this collaboration, the Center is also working with the Florida State University Center for Advanced Power Systems and the Center for Economic Forecasting and Analysis to support their Superconductivity Outreach Center. Tim Lynch from CEFA will brief 60 to 80 teachers at the Center's winter

Ambassador meeting in addition to providing display materials for the April 2004 National Science Teachers Association conference in Atlanta.

Hydrogen technology has recently become an area for scientific and engineering inquiry as well as a hot news item (The New York Times, November 4, 2003). The NHMFL/FSU has agreed to be part of a consortium to establish a Southeast Hydrogen Technology Learning Center. The purpose of this Center is to educate the public concerning the long-term benefits of a hydrogen economy. Educational programs at the NHMFL will focus on curriculum development. Consortium members include the University of Tennessee, Oak Ridge National

Laboratory, North Carolina State University, the Virginia Center for Coal and Energy Research at Virginia Tech, and others.

In addition to expanding into new directions this fall, the Center continues to provide quality educational outreach to K12 students coordinated by Carlos Villa. By the end of the fall semester, outreach will have been provided for over 6,700 K12 students! The CIRL team is also busy developing workshops and programs for summer institutes for teachers and preparing for the recruitment phase of our signature programs – REU and RET.

For further information about the NHMFL Center for Integrating Research and Learning, contact the program director, Dr. Pat Dixon, pdixon@magnet.fsu.edu, 850-644-4707.

A $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$ Superconducting Insert Magnet Generating 5.11 T in a 19.94 T Background Field—the World’s First Magnetic Field > 25 T from a Superconducting Coil

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A 25.05 T magnetic field was generated by a 5.11 T superconducting $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$ insert magnet within the large bore resistive magnet (LBRM) operating at 19.94 T. This is the first time that a magnetic field greater than 25 T has been generated using superconductivity. The $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$ magnet is constructed using fully reacted powder-in-tube conductor and insulated stainless steel reinforcement. Three concentric sections are used to minimize the total stress in the $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$ conductor; two double-pancake stacks and an outer layer-wound section. The insert coil was tested at 4.2 K in a 168 cm diameter cryostat fitted to the LBRM. Performance was limited by quenching. Here, we provide an overview of the design and construction of the insert and test results.

Introduction

One of the initial charges to the NHMFL in the founding operating agreement with the NSF is the development of state-of-the-art superconducting magnets that generate magnetic fields greater than 25 T. Technology based on metallic low temperature superconductors (LTS) exists for NMR magnets generating over 21 T, with 23.5 T NMR magnets currently under development.¹ Although the maximum field that may ultimately be generated by LTS magnets is not known with certainty, the magnetic field dependence of their critical current density is increasingly limiting at higher fields and prospects for further, significant improvements are limited by H_{c2} . Technical high temperature superconductors (HTS) at liquid helium temperature do not have such an intrinsic limitation and show large current density with minimal magnetic field dependence in magnetic fields over 20 T,² and thus have the potential of generating magnetic fields well beyond 25 T.³

Here, we report on the successful testing of a $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$ (Bi2212) insert coil that generated 5.11 T in a 19.94 T background field. Thus, for the first time, a magnetic field >25 T has been generated with a superconducting magnet. This insert coil represents a significant step toward 25 T superconducting research and NMR magnets. The NHMFL Large Bore Resistive Magnet (LBRM)^{4,5} generated the 19.94 T background magnetic field. Here, the HTS insert coil is discussed, including the design, construction, safety, and test results. More details can be obtained in references 6 and 7.

HTS Insert Coil Design Concept

The HTS insert coil design is driven by a number of aspects including previous experiences in the development, construction, and testing of high field insert coils.⁸ The insert coil is built with three concentric sections; the innermost (A) and middle (B) sections are built using stacks of double pancakes, and the outermost (C) section is layer-wound. The diameter of the free bore of the innermost section is 38 mm, representing a sufficiently large bore to support research usage. All sections are constructed using the react-and-wind approach. During final assembly, all sections are connected in series electrically. The outer diameter of the outermost coil must be such that the entire insert coil assembly can be tested within the 168 mm bore of the cryostat specifically built for testing coils within the LBRM. A $1 \mu\text{V}/\text{cm}$ electric field criterion is used to define critical current for short samples of conductor, individual double pancakes, and for the entire insert coil. Details of the Ag-alloy clad, powder-in-tube Bi2212 conductor manufactured by Oxford Superconducting Technology have been described previously.⁹ The conductor cross-section is 5mm wide x 0.2 mm thick and contains 19 Bi2212 filaments. Irreversible strain degradation under uniaxial tensile loads at 77 K occurs at strains of $\sim 0.4\text{--}0.5\%$.¹⁰ Limiting the radial build of each coil section such that the peak strain $\leq 0.36\%$ drove the design. Note that the net strain is the sum of bending strain from winding and Lorentz-force induced strain during operation. Stainless steel tape of 27 μm thickness, with a ceramic coating to provide electrical insulation, was co-wound with the Bi2212 conductor.

The critical current (I_c) of Bi2212 is anisotropic with respect to the angle between the magnetic field and the conductor, whereby the perpendicular field component dominates I_c .¹¹ With the insert generating 5.11 T in a 19.94 T background, the maximum effective perpendicular field is 2.54 T. It is thus worthwhile to optimize the double-pancake stacking order to benefit from the existing variations in B_{eff} .¹²

In the 3 T insert magnet reported previously,⁸ all three concentric sections were constructed from stacked double-pancake coils. The production process for double pancake units follows the react&wind approach, using a continuous piece of reacted conductor co-wound with insulated steel and subsequent vacuum impregnation with unfilled Stycast 1266 epoxy. A 25 to 50 μm Kapton layer separates the pancake halves. During stacking, selected units are painted with filled Stycast 2850 on the inner diameter and top/bottom surfaces before mounting on the bore tube. A sheet of Kapton provides a continuous insulation layer between units.

The C-coil is constructed using layer-winding. This option became viable because sufficiently long batches of reacted conductor of ~ 70 m each became available allowing for a minimum of resistive joints within the coil. This provided the opportunity to evaluate layer-winding technologies for high-field Bi2212 inserts. Three internal, resistive lap

TABLE 1. Geometric and related parameters of the Bi2212 insert coil.

	Unit	A section	B section	C section
Inner radius	mm	20.5	53	78
Outer radius	mm	48	73	82.5
Total height	mm	185	185	209
Construction	-	17 double pancakes	17 double pancakes	14 layers
Total # turns	-	3723	2611	532
Conductor length	m	801	1034	268
Coil constant	mT/A	24	15	3
Self Inductance	H	0.23	0.39	0.03
Packing factor*	-	0.71	0.71	0.5
Resistive joints	-	16	16	3

* total conductor cross section as a fraction of the winding cross section

joints of 8 cm length and a 4.2 K resistance of 15 n Ω joined four batches of conductor. The total length of conductor is 269 m. Layer-to-layer electrical insulation and mechanical reinforcement was obtained by co-winding tape-on-tape with 27 μm thick stainless steel, which had been previously coated with a ~ 10 μm thick layer of MgO doped ZrO₂.¹³ Turn-to-turn insulation within a layer was accomplished by a Kevlar thread of 0.2 mm diameter running between the turns.

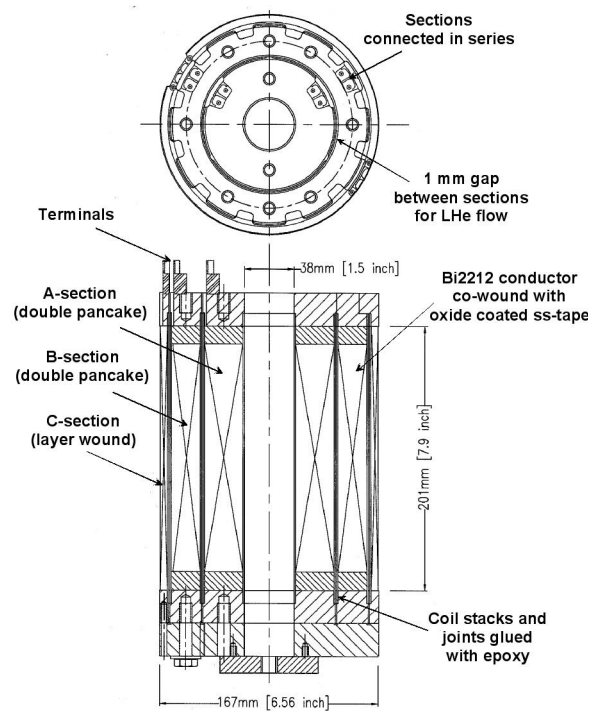
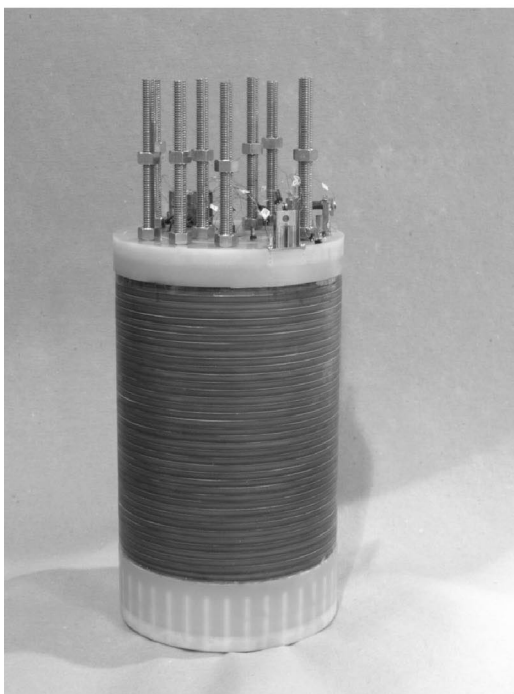


Figure 1. Photograph and schematic cross-section of the Bi2212 insert coil.

Joints between double pancakes are five or six pieces of Bi2212 tapes soldered axially and parallel to each other. The steel reinforcement tape was removed from the joint/lead areas to facilitate electrical contact. Insulation and reinforcement of every joint and lead connection were accomplished with a layer of glass fiber and Stycast 2850 epoxy, as well as by overlapping the ends of the steel tape.

The Bi2212 insert coil is instrumented with multiple voltage taps, including one across each section. A Hall sensor is placed at center field. The Hall sensor is calibrated against the current in the LBRM, for which the field-current relation is known with a relative error $< 10^{-3}$.

As-Built Insert Coil Parameters

A and B double pancake sections

Prior to A- and B-coil assembly, every double pancake unit is tested at 4.2 K, self-field. In addition, several units are selected for testing in high background magnetic field to verify stress tolerance and field dependence of I_c . From the measured $I_c(B)$ dependence and the calculated design operating current of 126 A (to generate 5 T) the required minimum self-field I_c values of 224 A for A-units and 238 A for B-units are obtained. If all double pancake units exactly meet these criteria, the projected I_c (19 T) corresponds to a magnetic field generation in the HTS insert of 5 T. As there is a distribution of self-field I_c values for the double pancakes, optimization of the stacking order is required to maximize the field generation. The optimum is reached when the anticipated reduction in overall stack I_c resulting from adding an additional double pancake with the next-lowest I_c exceeds the increase in field constant obtained by having a longer solenoid. Table 1 presents the main parameters for the entire insert. The insert coil and a schematic of its cross-section are shown in Figure 1.

The insert coil design was based upon a maximum background magnetic field from the LBRM of 19 T. If no other resistive magnets are being operated in the NHMFL DC facility, however, it is possible to operate the LBRM at 19.94 T reliably for extended periods of time. This corresponds to a 4-5% increase in stress and strain in the insert coil, reducing the safety margin relative to the onset of strain-induced permanent degradation from $>10\%$ to $>5\%$ of the design insert current.

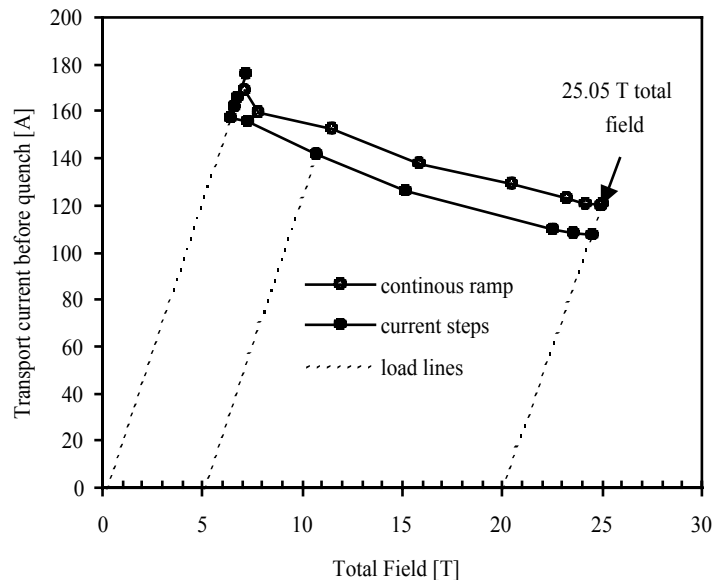


Figure 2. Bi2212 insert coil current before quenching versus the central magnetic field (LBRM plus insert coil). Some of the HTS insert coil load lines are included to differentiate the contributions of the background magnetic field and the insert coil.

Results

After wiring the A, B, and C coils with voltage taps, strain gauges, and the Hall sensor, assembling the double-pancakes into the A- and B-stacks, and combining the three sections into one coil, the entire insert was cooled to 4.2 K. The first self-field measurement was performed using a step-and-hold approach for the transport current. During these measurements a thermal runaway occurred several seconds after increasing the current above 176 A, at a central field of 7.2 T, and the magnet quenched with the overall electric field below $1 \mu\text{V}/\text{cm}$. Extrapolation of the measured raw data yields an intercept with the $1 \mu\text{V}/\text{cm}$ criterion at 208 A. Subsequent measurements with smaller current steps when approaching the quench current (I_q) show a reduction in quench current.

The step-and-hold approach was also used for testing the insert coil in background fields up to 19.94 T. In all cases, a thermal runaway, initiated in the A-section, occurred before the $E=1 \mu\text{V}/\text{cm}$ criterion was reached in any section of the insert coil. Figure 2 presents the highest current values before thermal runaway occurred. An increase of 1 A from these values results in the onset of thermal runaway, as observed by an increase in power supply output voltage at

Table 2. Performance of the HTS insert in the 19.94 T background magnetic field.

	A-stack	B-stack	C-coil	whole insert
Maximum operating current	120.4 A	>120.4 A	>120.4 A	120.4 A
Average current density @I=120.4 A	89 A/mm ²	87 A/mm ²	69 A/mm ²	86 A/mm ²
Field increment	2.9 T	1.8 T	0.31 T	5.11 T
Stored energy				9.7 kJ
Maximum axial field	25.05 T	22.24 T	20.47 T	
Maximum radial field	1.81 T	1.99 T	2.06 T	
Maximum Beff	2.51 T	2.59 T	2.57 T	
Average Lorentz-force induced stress	72 MPa	116 MPa	115 MPa	
Max bending strain	0.11%	0.044%	0.03%	

constant current. An additional few seconds is required for the output voltage to reach its trip value of 8 V. The field dependence of the quench current implies that the quench is caused by a section of conductor reaching I_c and is not mechanical in origin. If conductor motion were the cause, quenches would occur at fixed or decreasing values of the product of magnetic field and insert current, which was not observed.

Changing the measurement procedure from current step-and-hold to constant current ramp rate results in higher quench currents. Using a 3.7 A/s ramp rate for the insert in a 19.94 T background magnetic field resulted in a quench for an insert current of 120.43 A, corresponding to a central field of 25.05 T. Reproducibility of this result indicates an absence of Lorentz-force induced degradation. This represents the first time an HTS insert magnet, in combination with an outsert, generates a central field >25 T. Additional parameters for the insert, including details of the three sections, are in Table 2. Reducing the background field to 18 T increases the generated field just before quench to 5.2 T. This is the largest field increment generated by an HTS insert magnet at high magnetic field¹⁴ with a useable bore (somewhat arbitrarily defined as >30 mm).

The average stress from Lorentz forces on the midplane of each of the three sections is estimated from the product of current density, magnetic field, and radius for a point

halfway between the inner and outer radius. The results are listed in Table 2. The peak value may exceed the average by as much as 50% for the A-section. Bending strain is the second-largest source of strain and is listed separately. Differential thermal contraction between reinforcement and conductor is considered negligible compared to Lorentz-force and bending strain. The highest stress and strain occur with the insert and outsert combined to generate 25.05 T with 120.4 A in the insert. Reproducibility of this quench current indicates that the strain in the insert is everywhere below the critical strain and the reinforcement is adequate.

Conclusions

The design, construction, and test results of a react-and-wind Bi2212 insert magnet consisting of two stacks of double-pancakes and an outer layer-wound section, featuring co-wound ceramic-coated stainless steel for reinforcement and insulation, are presented. The insert magnet generates 5.11 T in the presence of a 19.94 T background magnetic field, resulting in a combined magnetic field of 25.05 T. This is the first time a superconducting insert magnet operated with a central field of greater than 25 T. This is a significant milestone toward 25 T superconducting magnets. This is also the highest field increment for an HTS insert with a bore greater than 30mm. The inclusion of co-wound, insulated stainless steel is effective; neither strain-induced degradation nor electrical shorting is observed.

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NEWS from AMRIS

The Advanced Magnetic Resonance Imaging and Spectroscopy Facility at the University of Florida

MRI Monitoring of Stem Cell Therapy

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B.J. Byrne, UF, Pediatrics and Molecular Genetics and Microbiology; and Powell Gene Therapy Center

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T.N. Frimel, UF, Physical Therapy

G.S. Gaidosh, UF, Physiology and Functional Genomics

With new potential therapies on the horizon, there is an urgent need for noninvasive imaging modalities to study muscle function. Gene and/or stem cell transfer, two therapeutic strategies that may have tremendous therapeutic potential, currently rely heavily on invasive techniques. This is problematic when attempting to evaluate these therapies in the clinical setting involving patients with extensive muscle damage or during muscle senescence. Therefore, it is imperative to develop noninvasive techniques capable of providing high-resolution images of muscle at the cellular level. Current work performed in the AMRIS facility focuses on the development of magnetic resonance spectroscopy (MRS) and imaging (MRI) techniques that allow for the noninvasive monitoring of gene transfer efficacy and stem cell delivery methods. Widespread gene expression can be achieved in adult cardiac and skeletal muscle using either recombinant adeno or adeno-associated viruses. We have previously found that MRI/MRS methods can be used to monitor the expression of a MR marker gene (arginine kinase)¹ and therapeutic genes for the muscular dystrophies and cardiomyopathies.² On the other hand, cell based therapies may represent a greater challenge for noninvasive monitoring due to the wide variability in stem cell incorporation.

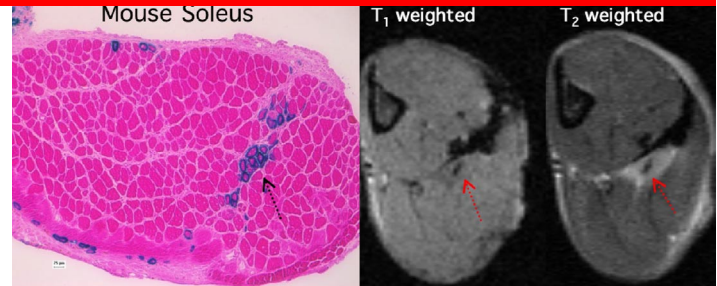


Figure 1. (Left) Histological verification of muscle stem cell integration into the mouse soleus following muscle damage by X-gal staining of the LacZ expressing cells (blue). (Right) Labeled cells result changes in MR image contrast on both T1 and T2 weighted sequences. Note the hyper intense regions within the mouse soleus on T2 weighted images correspond to muscle damage prior to stem cell delivery.

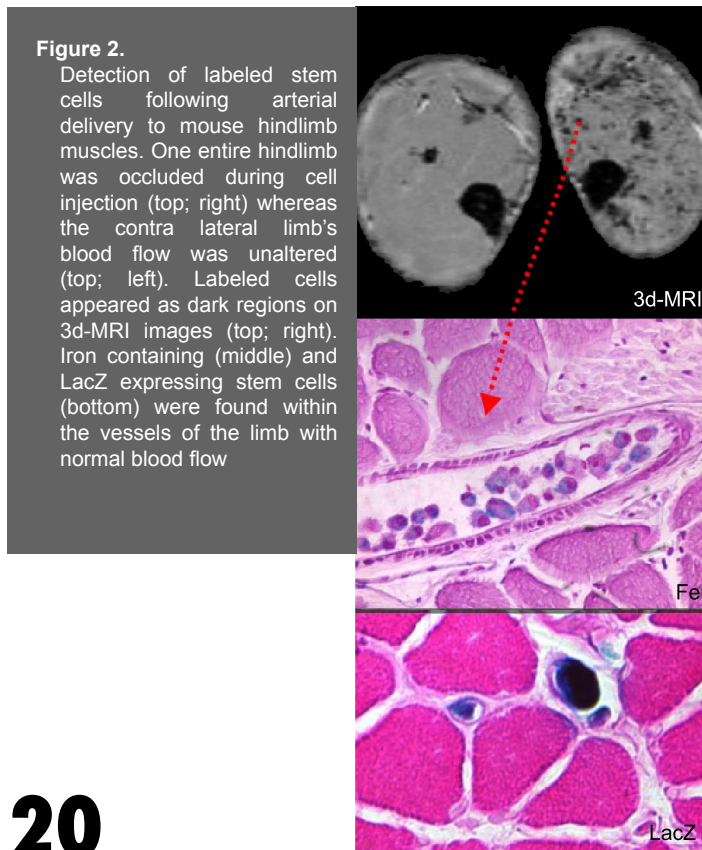
Recent interest has focused on the therapeutic use of stem cell transplants for diseases characterized by irreplaceable cell loss. The identification of novel populations of adult muscle stem cells capable of multi-potent differentiation and enhanced muscle regeneration has fueled new interest in the clinical promise of cell-based therapies for muscular dystrophy and muscle senescence.^{3,4} It is anticipated that such a population of adult cells can be isolated, modified to express therapeutic genes, and then reintroduced systemically. *In vivo* cell migration to damaged areas occurs by the local expression of endogenous chemotactic and mitogenic factors. We are addressing whether cell homing can be enhanced by the targeted expression of key chemotactic genes by recombinant viral techniques. In Duchenne's muscular dystrophy, for example, a mutation in the gene encoding the membrane protein dystrophin ultimately leads to the exhaustion of resident muscle progenitor cells in an attempt to replace damaged and dysfunctional muscle fibers. Once unable to further regenerate damaged fibers, the muscle is quickly infiltrated by connective tissue and fat.⁵ Therapeutic approaches have been designed to replace dysfunctional muscle fibers and complement dystrophin deficiency through the delivery of normal or genetically modified stem cells

capable of muscle fiber regeneration.⁶ A second example is senescent and damaged tissue in which resident stem cells may be exhausted or non-functional. In this experimental paradigm MR is used to determine whether the recruitment of endogenous and/or mobilized stem cells will increase the rate of muscle regeneration and improve muscle function.

Common techniques to monitor muscle stem cell transplants typically rely on *ex vivo* genetic modification to allow expression of reporter genes.⁷ The statement of specific reporter genes allows for graft identification during post-mortem analysis. Using these conventional techniques, however, even simple and practical questions are difficult and labor intensive to answer. For example, to determine the distribution of the graft, the entire organ must be harvested and sectioned, followed by identification of individual cells by conventional microscopy. More complex questions, such as cell homing, identification of migration events, and engraftment rates, may be impossible to accurately and quantitatively address using conventional microscopy. Novel techniques that allow non-invasive, continuous imaging of stem cell transplants have recently been proposed and evaluated in a limited number of cell delivery models.^{8,9} MRI imaging has the ability to provide extremely sensitive, high-resolution images of magnetically labeled cells. As such, the application of MR imaging to stem cell investigations is of great importance to enhance the development of stem cell therapies.

We are currently evaluating the application of magnetically labeled stem cells for monitoring therapeutic stem cell transplants in murine dystrophies¹³ and senescent muscle (Figure 1). Multipotent, muscle derived stem cells are labeled by incubation with ferumoxide:polycation complexes resulting in endosomal accumulation of supraparamagnetic iron-oxide. The presence of a small number of labeled cells causes large changes in MR contrast (decreased T_2 & T_2^*), allowing for three dimensional, non-invasive detection. Relaxativity measurements on cell phantoms demonstrate that MR imaging can be used to detect a single labeled cell. Furthermore, therapeutic cellular grafts transplanted into dystrophic muscle and normal murine muscles can be imaged sequentially, showing a strong spatial correlation between *in vivo* and *in vitro* indices of cell incorporation. Additional studies reveal that MR imaging can be implemented to track the migration of a small number of labeled cells following arterial delivery (Figure 2).

Targeting stem cells to the ischemic and damaged myocardium is of the highest priority. Cardiac dysfunction, resulting from various insults to the myocardium, can ultimately lead to the development of heart failure. The heart is at great risk of irreversible cell loss due to the limited regenerative capacity of adult cardiac tissue and the lack of a resident cardiac progenitor cell equivalent to the skeletal muscle satellite cells. The transplantation of myogenic cells into the myocardium has been investigated as a novel mechanism to repair damaged and dysfunctional myocardium.¹⁰ Skeletal myoblasts are a committed progenitor cell population found in close proximity to the mature skeletal myocytes.¹¹ This cell population can be easily isolated from an adult muscle biopsy and propagated in tissue culture. Numerous reports have documented the ability of skeletal myoblasts to survive in healthy as well as damaged myocardium and ultimately improve systolic and diastolic function.¹² Again progress in the development and implementation of stem cell transplants as clinical therapies has been delayed by limitations in post-mortem analyses. MR cardiac imaging has the dual advantage of being able to provide high-resolution images that not only offer structural information, but can be further utilized to provide indices of global and regional cardiac function. We have demonstrated that small numbers of magnetically labeled myoblast grafts can be detected in rodent myocardium following transplantation (Figure 3). The non-invasive analysis of myoblast grafts will be important in clinical studies to readily determine the relationship of the graft to cardiac function.



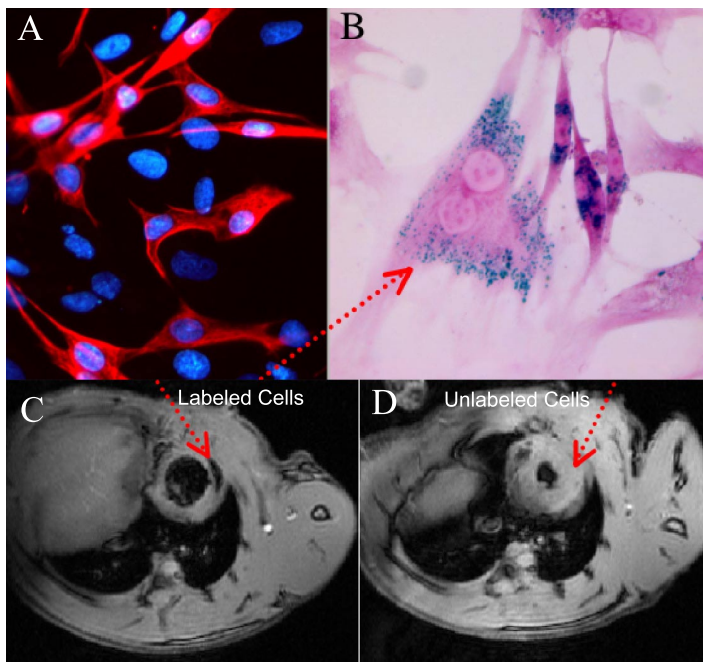


Figure 3. (A) Desmin expression (red) by primary rat myoblast cultures after 5 days of culture. (B) Prussian blue stain of undifferentiated following ferumoxide-PLL labeling. Short axis (C&D) MRIs of labeled (C) and unlabeled (D) myoblast transplants in viable rat myocardium 24hrs post-injection.

We conclude that MR monitoring of contrast agent loaded cells is particularly well suited for investigations involving the vascular delivery of stem cells and other delivery strategies that rely on stem cell homing to the site of injury. This MR technique utilizes FDA approved contrast agents, is widely accessible, and may permit continuous, non-invasive readout of cell transplants in cardiac and skeletal muscle.

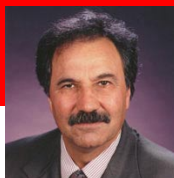
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PEOPLE IN THE NEWS



R. Abbaschian

C. Hendrickson

D. Smirnov

D. Tanner

Gemesis, a private company founded at UF with the technical expertise of **Reza Abbaschian**, professor and chair of the UF Department of Materials Science and Engineering and member of the NHMFL extended family was featured in *Wired Magazine*. With Abbaschian's help, Gemesis has become the first company to market gem-quality synthetic stones made by man-made heat and pressure. Diamonds are highly effective semiconductors capable of operating at higher power and temperatures than traditional silicon semiconductors. This summer, Abbaschian, a University of Florida Vladimir A. Grodsky Professor, received the 2003 American Society for Engineering Education Donald E. Marlowe Award in recognition of his distinguished accomplishments. Under his leadership, the materials science program at UF has risen from 35th to 10th among all public and private universities, according to *U.S. News & World Report*. Abbaschian received his B.Sc in Mining and Metallurgy from Tehran University and his Ph.D. in Materials Science and Engineering from the University of California, Berkeley. The emphasis of his research has been in the fundamental understanding of the role of interfaces on the processing and/or properties of material.

Chris Hendrickson, associate director of the ion cyclotron resonance program at the National High Magnetic Field Laboratory and courtesy professor of chemistry at Florida State University, was named to the "A-page Advisory Board" for Analytical Chemistry. He received his B.A. degree in chemistry from the University of Northern Iowa and his Ph.D. in analytical chemistry from the University of Texas at Austin. His research interests are in instrumentation, technique development, and applications of analytical Fourier transform ion cyclotron resonance mass spectrometry.

Dmitry Smirnov has joined the Instrumentation & Operations Group at NHMFL/Tallahassee. Smirnov is in the User Support group as a visiting assistant scholar scientist. He graduated from Leningrad Electrical Engineering Institute in St. Petersburg, Russia in 1988 and received his Ph.D. at the A.F. Ioffe Physico-

Technical Institute of the Russian Academy of Sciences in St. Petersburg in 1996. He has worked at the Ioffe Institute, and the French National Pulsed Magnetic Field Laboratory in Toulouse, France.

Smirnov has been involved in developing far-IR detectors for space-borne instruments. He specializes in IR magneto-optics. His general interests include optical and transport properties of low-dimensional semiconductor structures and optical conductivity studies of correlated fermion systems. At the NHMFL, Smirnov will work with users and develop instrumentation for magneto-optical experiments in the region from middle-IR to very far-IR (THz). His personal research will focus on inter-subband transitions in semiconductor cascade nanostructures.

David Tanner, UF professor of physics, has been elected the vice chair of the Division of Condensed Matter Physics by the American Physical Society. He will assume the office of vice chair at the March 2004 meeting of the society in Montreal. He will serve as chair elect in 2005 and chair in 2006. Tanner received his B.A. in physics from the University of Virginia and his Ph.D. in physics from Cornell University. His research interests include the study of materials by optical reflectance or transmittance at wavelengths from the far infrared through the near ultraviolet, and a full-scale dark-matter axion search at Lawrence Livermore National Laboratory with Pierre Sikivie and Neil Sullivan.

Xiaoming Wang has joined the Instrumentation & Operations Group at NHMFL/Tallahassee. Wang is a visiting graduate student. He is from Beijing, China and graduated from Tianjin University, Department of Applied Physics with a BS and MS. He spent three years working as a research assistant studying crystal growth and properties at the Institute of Physics at the Chinese Science Academy. He is presently working on his Ph.D. with David Reitze in the Physics Department of the University of Florida. They are developing and using instruments for ultrafast spectroscopy in condensed matter physics.

CONFERENCES & WORKSHOPS

Events for 2004

5th Biennial Structural Biology Symposium Membranes: A Challenge for Protein Magnetic Resonance

<http://www.sb.fsu.edu/conference/>

January 23-24, 2004

Tallahassee, Florida

Contacts:

Tim Cross (cross@magnet.fsu.edu, 850-644-0917)

Peter Fajer (fajer@magnet.fsu.edu, 850-644-2600)

44th Sanibel Symposium

<http://www.qtp.ufl.edu/~sanibel/>

February 28-March 6, 2004

St. Augustine, Florida

Contact: sanibel@qtp.ufl.edu

International Workshop on Materials Analysis & Processing in Magnetic Fields

March 2004

Tallahassee, Florida

Contact: Hans Schneider-Muntau

(smuntau@magnet.fsu.edu, 850-644-0863)

Fluctuations and Noise in Materials

<http://spie.org/Conferences/Calls/04/fn/conferences/index.cfm?fuseaction=FN03>

May 25-28, 2004

Maspalomas, Gran Canaria, Spain

Contact: Dragana Popović

(dragana@magnet.fsu.edu, 850-644-3913)

16th International Conference on High Magnetic Fields in Semiconductor Physics (SemiMag16)

<http://SemiMag16.magnet.fsu.edu>

August 2-6, 2004

Abstract Deadline: April 2, 2004

Early Registration Deadline: June 25, 2004

Tallahassee, Florida

Contact: Yong-Jie Wang

(SemiMag16@magnet.fsu.edu, 850-644-1496)

Applied Superconductivity Conference (ASC04)

<http://www.ASCinc.org> (under development)

October 4-8, 2004

Abstract Deadline: March 15, 2004

Jacksonville, Florida

Contact: Justin Schwartz

(ASC04ConfChair@magnet.fsu.edu, 850-644-0874)

15th Conference of the International Society of Magnetic Resonance (ISMAR 2004)

<http://www.ismar.org/>

October 24-29, 2004

Ponte Vedra Beach, Florida (near Jacksonville)

Contact: Tim Cross

(mail@ismar.org, 850-644-0917)

Events for 2005

Physical Phenomena at High Magnetic Fields – V (PPHMF-V)

August 5-9, 2005

Tallahassee, Florida

Contact: Coordinator Alice Hobbs

(aclark@magnet.fsu.edu, 850-644-3203)

24th Low Temperature Physics Conference (LT-24)

August 10-17, 2005

Orlando, Florida

Contact: Gary Ihas

(ihas@phys.ufl.edu, 352-392-9244)

Other Meetings of Interest

5th International Conference on the Scientific and Clinical Applications of Magnetic Carriers

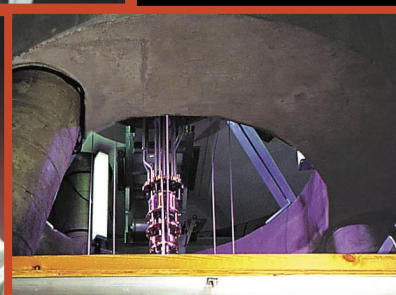
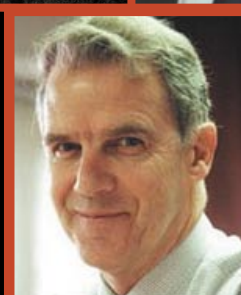
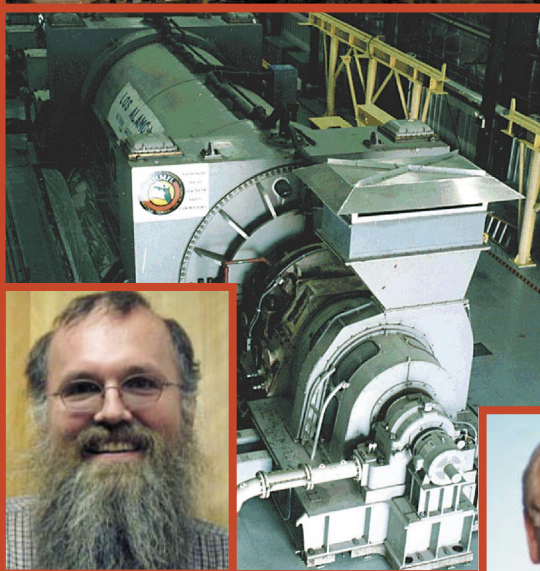
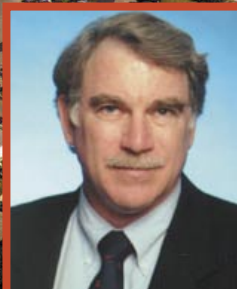
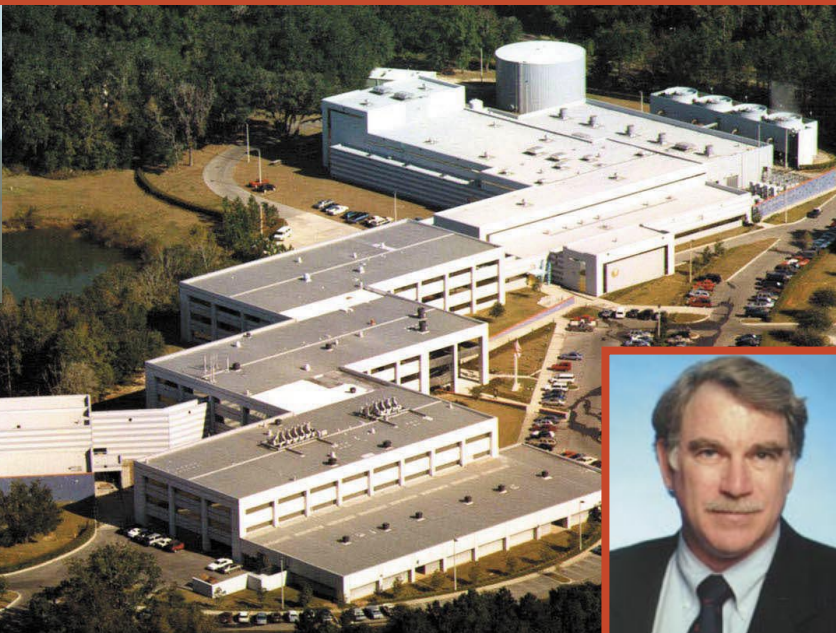
<http://www.magneticmicrosphere.com/meet2004.htm>

May 20-22, 2004

Registration & Abstract Deadline: March 12, 2004

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Top Left Corner: Jack Crow, NHMFL Director and Principal Investigator (PI), and aerial view of the National High Magnetic Field Laboratory at Florida State University, Tallahassee. Top Right: Alan Marshall, ICR Program Director and PI, NHMFL-FSU. Middle Right: Neil Sullivan, PI for the NHMFL at the University of Florida, and views of the High B/T Facility at UF (see also the Front Cover for results from research conducted at the AMRIS Facility at UF). Bottom Left: Greg Boebinger, PI for the NHMFL at the Los Alamos National Laboratory, along with picture of the 600 megajoules AC generator. Center: Bob Schrieffer, Nobel Laureate and NHMFL Chief Scientist.