# Intranuclear Gadolinium in Glioblastoma Cells for Neutron Capture Therapy

Glioblastoma is the most lethal and incurable brain cancer, with 12,000 victims per year in the US, and more than 200,000 worldwide. This malignancy is resistant to chemotherapy, surgery and radiotherapy. Novel efforts, such as gadolinium neutron capture therapy (GdNCT) have been proposed, but their efficacy has yet to be proven in animal or human cases. The GdNCT non-invasive modality, is based on two steps: (i) inject a tumor-seeking $^{157}$Gd compound to patient; (ii) bombard the skull with thermal neutrons. Upon neutron capture, electron emission can induce cell death provided that Gd be in the proximity of DNA, that is, in the cell nuclei of glioblastoma cells. GdNCT was first suggested in the 1980s, but lack of evidence for intranuclear Gd uptake impeded its development. G. De Stasio and her group at the UW-Synchrotron Radiation Center first observed preferential Gd uptake in cancer cell nuclei, after exposure of the cells to a Gd compound: Gd-DTPA (De Stasio et al., Cancer Research, **61**, 4272-7, 2001).

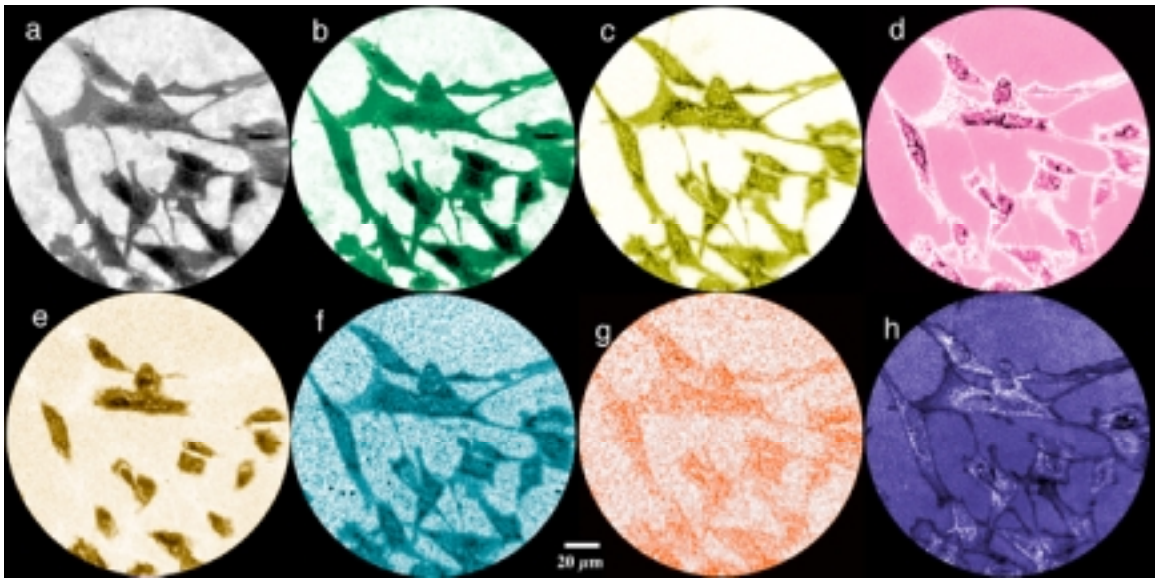



Figure 1. (a) Photoelectron micrograph of human glioblastoma cells grown on a flat silicon substrate. The micrograph was acquired with 1200 eV photon energy illumination by the **SPHINX** spectromicroscope at the Wisconsin Synchrotron Radiation Center, on the **HERMON** beamline. The beamline with its broad energy range (60-1300 eV), and the microscope with the record resolution of 5.5 nm, are **unique in the world**. (b) Phosphorus distribution map in the same group of cells. (c) Ca distribution map. (d) S distribution map. (e) C1s map. (f) K2p map. (g) Na1s. (h) Cl map. In all distribution maps, black or dark color indicates higher element concentration, white corresponds to no element. All of these of elemental images cannot be obtained with any other single instrument.

They now extended the synchrotron x-ray spectromicroscopy experiments to 3 more Gd compounds: the Gd micro-distribution at the subcellular level was observed in human

glioblastoma cultured cells exposed to each drug (De Stasio et al, J. Rad. Oncol., submitted).

A critical evaluation of the results revealed that after exposing cells to MGd, Gd-DOTA and HM-Gd-DOTA there is striking specificity for nuclei in two cases (91% for MGd and 100% for HM-Gd-DOTA).

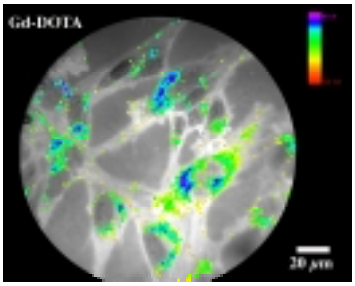



Figure 2. Gd maps acquired with SPHINX from human glioblastoma cells in vitro, exposed to Motexafin Gd (left), Gd-DOTA (center) and HM-Gd-DOTA (right). The total number of nuclei taking up Gd was counted on these and several hundreds of other similar Gd maps.

Prof. De Stasio actively involves graduate and undergraduate students in her experiments at SRC. Her group includes Bradley H. Frazer, UW-Physics and EPFL, Brandon R. Sonderegger, UW-Biophysics, Andrew Gadtke (UW-Physics undergraduate) and Lisa Wiese, SRC beamline scientist. Most recently she hosted Katherine Richter, an NSF-REU student from South Carolina. Katie was an exceptional acquisition to the group, and she was enthusiastically encouraged to join the group as a graduate student after she will have completed her undergraduate studies in 2003.

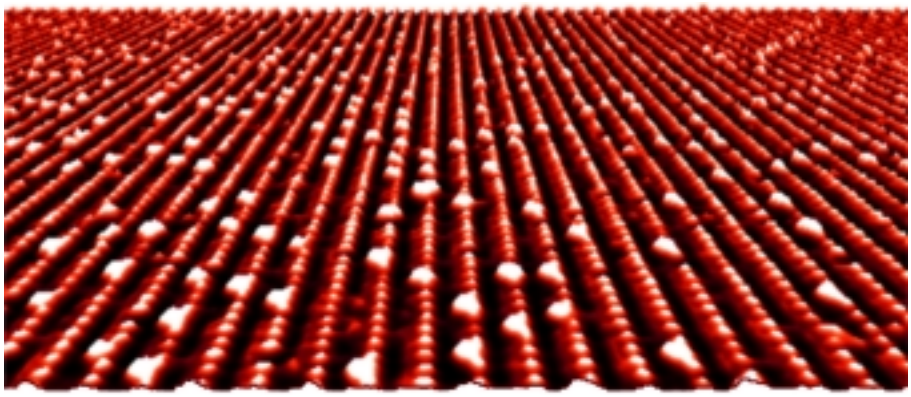
The spectromicroscopy program at SRC is involved in outreach activities and demonstrations, during the yearly Open House, and the frequent “around-the-vault” tours. De Stasio’s graduate/undergraduate “Microscopy of Life” class at UW-Madison, as well as the Wisconsin Center for Academically Talented Youth, both offered hands-on experience with the SPHINX microscope to the students, who are from 9$^{th}$ grade through Ph.D. level.

**Photoelectron Spectroscopy of Atomic Wires**

The properties of electrons become more and more exotic when progressing from the three-dimensional world into lower dimensions. Already in a two-dimensional electron gas surprising phenomena have been observed, such as fractional charge in the fractional quantum Hall effect. Two Nobel prizes have gone to research on two-dimensional electrons. Predictions for electrons in a one-dimensional wire are even more exotic. The concept of a single electron becomes obsolete because electrons cannot avoid each other along a one-dimensional track and become excited collectively. An even stronger prediction exists for a one-dimensional metal, where electrons separate into two quasi-particles, a spinon that carries spin without charge, and a holon that carries the positive charge of a hole without its spin.

One might think that the ultimate nanowire would be a single string of atoms suspended freely in space. However, according to a fundamental theorem by Peierls, the atoms in such strings always form pairs and lose their metallicity. Chains of metal atoms can now be assembled at stepped silicon surfaces, where they line up parallel to the step

**Fig. 1**



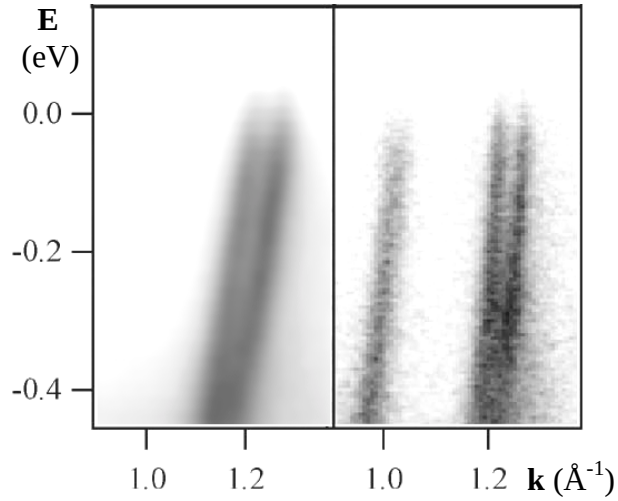
edges (Fig. 1). The atoms are locked to the silicon substrate crystal, which prevents them from forming Peierls pairs and losing their metallicity. Even though the metal atoms are locked to the silicon substrate, the electrons are de-coupled from it. A semiconductor, such as silicon, lacks metallic electrons to interact with. Thus, one has the best of both worlds, where atoms can be placed on a well-defined lattice and electrons remain free.

Photoemission experiments at the SRC by Renato Losio, Jason Crain, and coworkers in Franz Himpsel's group at the University of Wisconsin Madison have demonstrated that such chain structures can be metallic, indeed (Losio et al, Phys. Rev. Lett. **86**, 4632 (2001); Himpsel et al., J. Phys. Condens. Matter **13**, 11097 (2001)). In fact they are metallic despite an even number of electrons per atom, which would allow them to form electron pairs and become insulating. This can be seen in the band dispersion plots in Fig. 2, which combine the fundamental quantum numbers of an electron in a solid, i.e., energy E and momentum **k**. The dark E(**k**) curves extend all the way up to the Fermi level (E=0), where the electrons responsible for metallic conductivity reside.

On-going experiments continue to reveal new chain structures that are metallic, as demonstrated by two surfaces with different step density in Fig. 2. Both exhibit a closely-spaced pair of half-filled bands, but one of them has an additional band with quarter filling. Such variability creates opportunities for designing chain structures with variable

electron density and coupling. That should pave the way towards reaching exotic one-dimensional electron states, such as spinons and holons.

**Fig. 2**

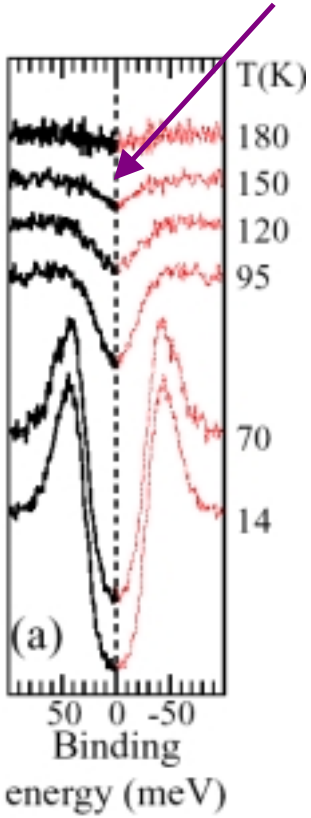



The measurements were obtained with a state-of-the-art spectrometer, which detects about 100 energies and 50 angles simultaneously. Such multi-detection allows the observation of E(**k**) plots in real time on a TV screen, 5000 times faster than conventional spectrometers which detect only a single E and **k**. The data in Fig. 2 are time-averaged screen images with black and white inverted. The panel on the left was taken at an undulator beamline, which delivers about twenty times more intensity than the traditional bending magnets (noisy panel on the right).

# Time reversal symmetry breaking in the high Tc superconductors

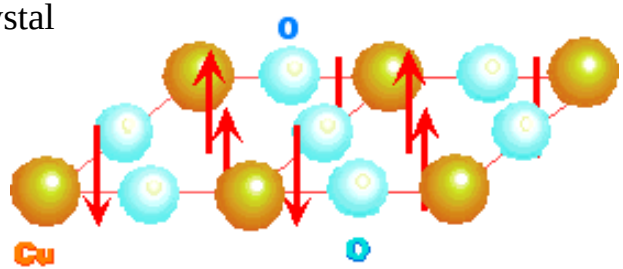
Juan Carlos Campuzano, University of Illinois at Chicago, DMR Award# 9974401

In 1996 the pseudogap in the high Tc superconductors was discovered in photoemission spectroscopy, where a electronic states start to dissapear in the normal state, before the superconducting gap appears at lower temperatures.

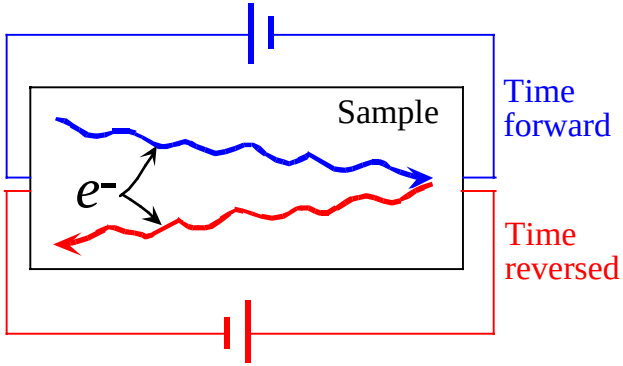



The big question: Is this due to some unknown order appearing in the material (none had been detected), or is the material just preparing to become a superconductor?

Some theories predicted that the pseudogap does represent the transition to a new phase, one in which microscopic magnetic fields appear in ordered patterns in the unit cell, the group of atoms that form the crystal




These fields **break time reversal symmetry,** that is, if a current is set up in the sample, the electrons traveling through in one direction are **deflected by the fields**. But if the movie is run backwards (**time is reversed**) the electrons do not return to their starting place



# Time reversal symmetry breaking in the high Tc superconductors

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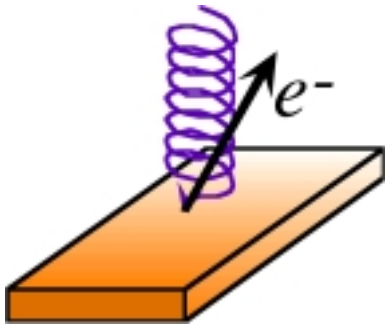
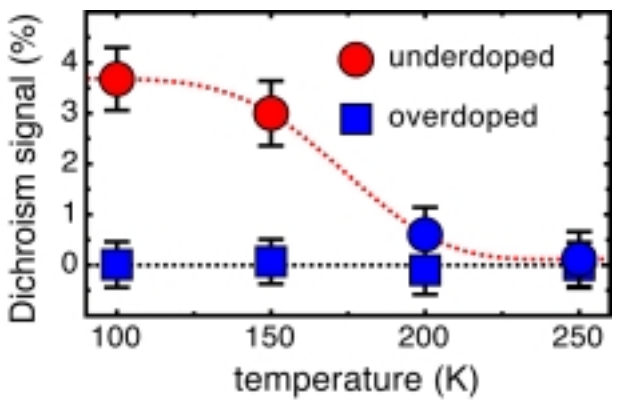
We have tested for time reversal symmetry breaking with angle resolved photoemission: by illuminating the sample with circularly polarized photons,

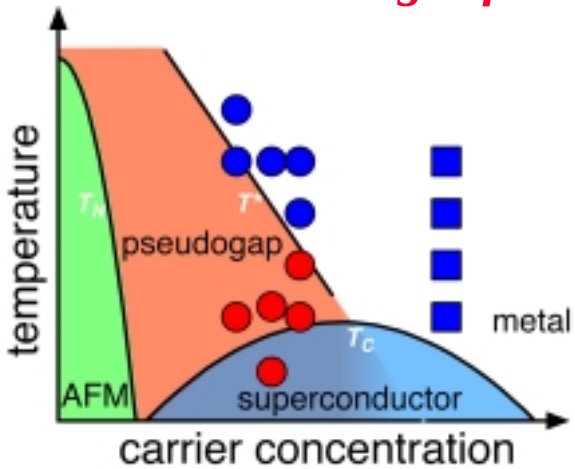



We find that the photocurrent with left polarized photons is not the same as that with right polarized photons, i.e. there is dichroism.




The dichroism appears as the pseudogap does, where a new type of order sets in. The blue dots in the phase diagram below indicate no dichroism, but the red dots indicate where we observe dichroism, where

***Superconductors can tell right from left!***

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