Introduction
Low sequence complexity domains in protein molecules were once disregarded as unstructured and unimportant for biological function. It is becoming increasingly clear that these domains are important for understanding mRNA processing and transport in healthy cells [1]. Furthermore, these domains are implicated in neurological diseases such as Amyotrophic Lateral Sclerosis [2]. This project focuses on the N-terminal low complexity domain of the Fused in Sarcoma (FUS) protein.

Experimental
The overall goal of the project is to determine the structure of fibrils formed by the FUS low complexity domain using solid state nuclear magnetic resonance (NMR). The first step in the structure determination process is to measure the $^{13}$C and $^{15}$N chemical shifts for the backbone atoms in the protein. We used the 21.1 T ultra wide bore NMR spectrometer at the NHMFL in Tallahassee, FL, to record 2D and 3D NC$_a$C$_x$ and NC$_n$C$_x$ spectra of the FUS fibrils. The high magnetic field provided increased spectral resolution and the state of the art probe technology developed by the RF group at the NHMFL increased sensitivity when compared to commercially available NMR spectrometers.

Results and Discussion
A 2D NC$_a$ spectrum of the FUS fibrils collected at the NHMFL is shown in Fig. 1. The spectrum exhibits a high signal to noise ratio and excellent resolution, indicating that the structure determination effort has a high probability of success. 3D experiments increase resolution and provide interresidue correlation information for $^{13}$C and $^{15}$N chemical shifts. Analysis of the data indicates that only 25% of the FUS low complexity domain is structured in the fibrils. Furthermore, the high quality spectra obtained have allowed sequence specific assignment of the chemical shifts into the FUS protein sequence.

Conclusions
The data obtained at the NHMFL has provided sequence specific assignments for the fibrils formed by the FUS low complexity domain. The next step in the structure determination process is the measurement of interatomic distance constraints. These experiments are ongoing.

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References