Department of Chemistry: Part III Project 2017/8

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Understanding molecular structures in tissues

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The extracellular matrix of structural tissues like bone, skin, tendon and vascular tissue is the primary material conferring the mechanical properties of the tissue. At least equally importantly though, the extracellular matrix plays a leading role in cell signalling through its binding to cells. The extracellular matrix is largely formed through self-assembly of proteins and other molecules into fibrils, networks and other structures and undergoes continual non-enzymatic chemistry throughout life, often with detrimental consequences. The matrix molecular assemblies in some way simultaneously provide highly specific protein binding sites for cell signalling and to maintain the wider structural integrity of the extracellular matrix, whilst at the same time are flexible, and thus necessarily dynamic structures, providing the essential tissue mechanics. How they do this, and how they are blocked from doing this by the chemistry that occurs in the matrix, is a central focus in our work.

The projects use advanced NMR methods along with electron microscopy to determine molecular structures in mammalian tissues in various contexts. Collagen is the most abundant protein in the extracellular matrix. One of the primary difficulties with engineering collagen *in vitro* for implants is knowing when the correct triple helical, cross-linked structure that occurs in Nature has been achieved. One project will work alongside an existing project to determine molecular structures of ^{13}C and ^{15}N enriched-collagens produced from cell culture and in small animal models, the latter being the first molecular structural characterization of intact tissues (Fig 1).

A second project will model the effects of cancer on tissues. All projects involve NMR experimental work, data analysis, simulation and optional synthetic work.

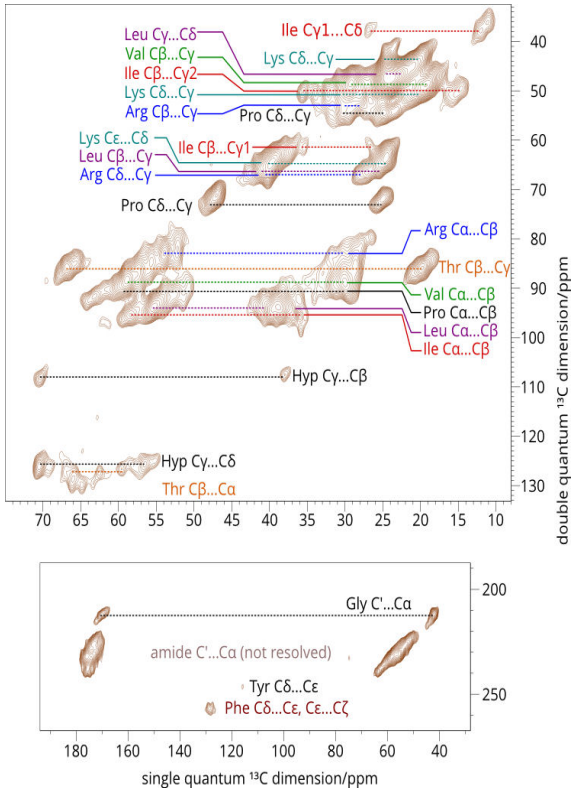

***Fig 1**: 2D single-quantum double-quantum ^{13}C-^{13}C through-space correlation SSNMR spectrum of the ^{13}C enriched mouse bone. The labels assign selected cross peaks to various amino acids. This is the first time that many of these signals for collagen have been assigned.*