Deep Learning Tools in NMR

Annual meeting of Managers of UK Magnetic Resonance Facilities

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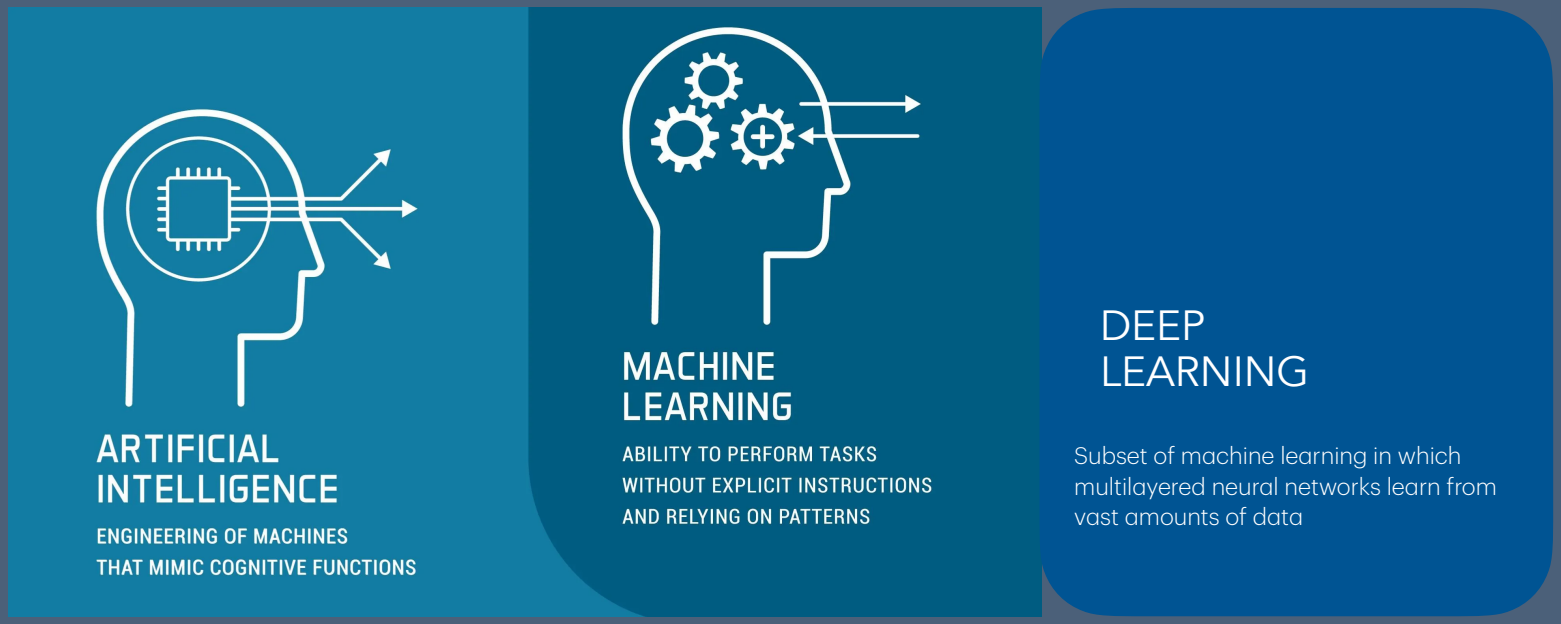
Introduction

AI, machine learning, and deep learning are interchangeable and easily confusing



A program that can sense, reason, act and adapt

Algorithms whose performance improve as they are exposed to more data over time

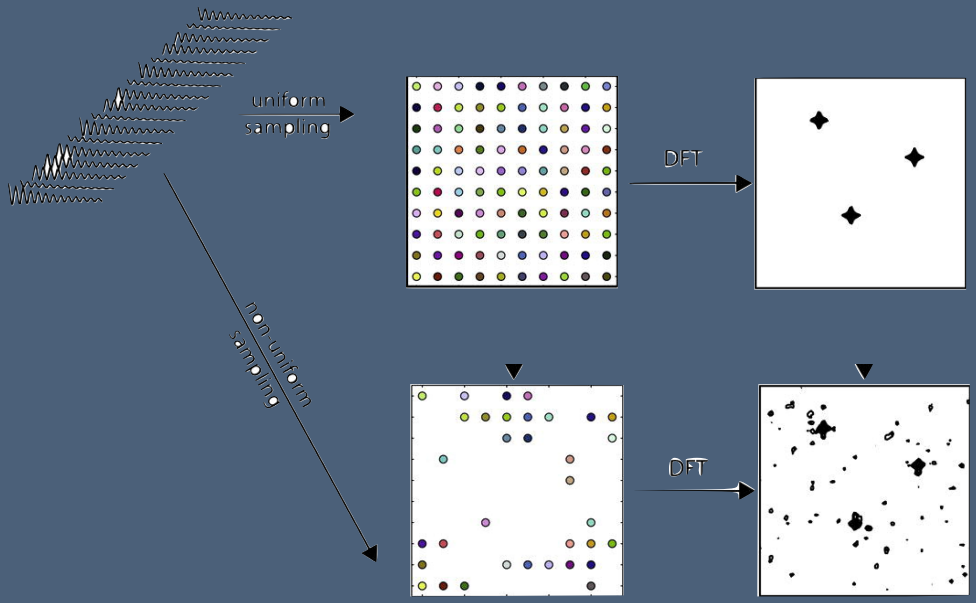
Over several decades ...

- Struggle to match human performance - intuitive human judgment
- Only on ‘perfect datasets’ - sharp well-resolved with minimal noise

Deep Learning

- Automate or improve different analysis stages
- Increasing efficiency, utility and ease of use of NMR spectroscopy

Reconstruction of non-uniformly sampled (NUS)



Several excellent algorithms for reconstructing NUS NMR spectra using non-DL methods:

- SMILE (Ying et al. 2017)

- hmsIST (Hyberts et al. 2012)

-MDD-NMR (Jaravine et al. 2006).

Recent proof-of-principles studies have shown that DL based reconstruction methods have the ability to give reconstructions more rapidly and with higher fidelity than existing methods

FID-Net

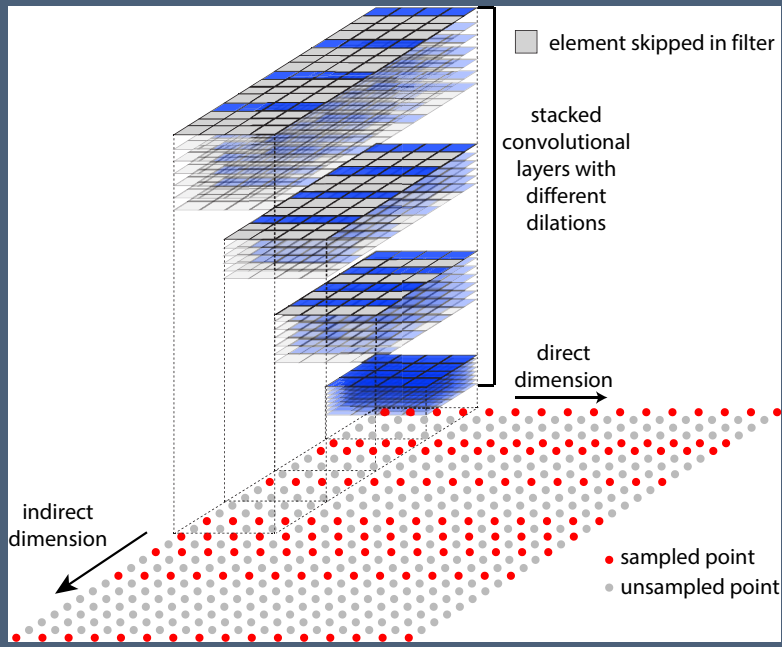
A versatile DNN architecture

FID-Net works effectively:

- arbitrary sampling schedules (meaning can be deployed w/o further training & minimal user input)

- processing time domain data beyond reconstruction tasks

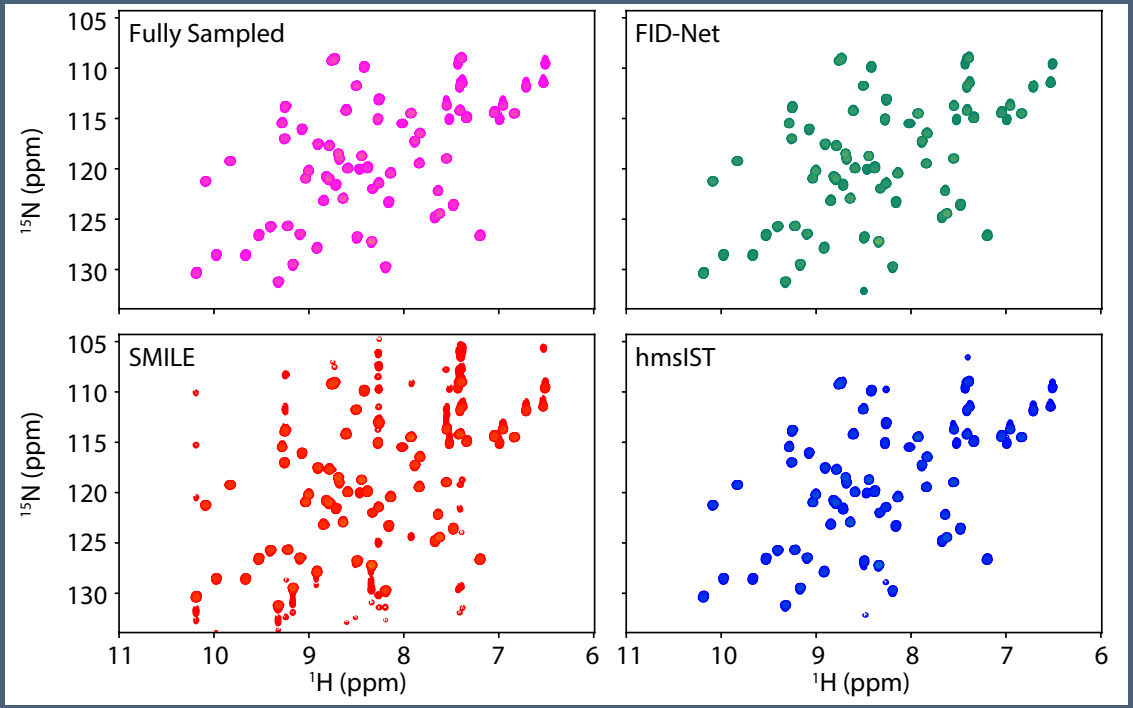
- Virtually decouple 13Cα-13Cβ couplings in HNCA spectra



Hansen DF, Journal Biomolecular NMR. (2021) 75:179-191

Reconstruction NUS spectra

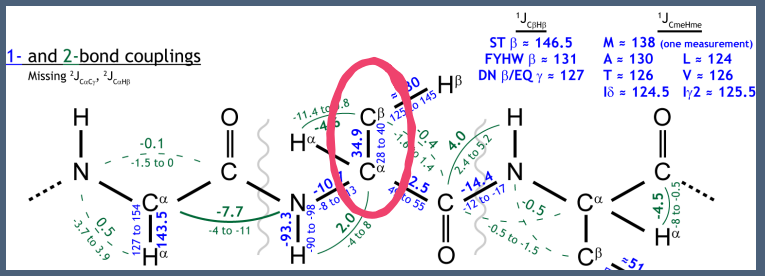
FID-Net *vs.* SMILE *vs.* hmsIST

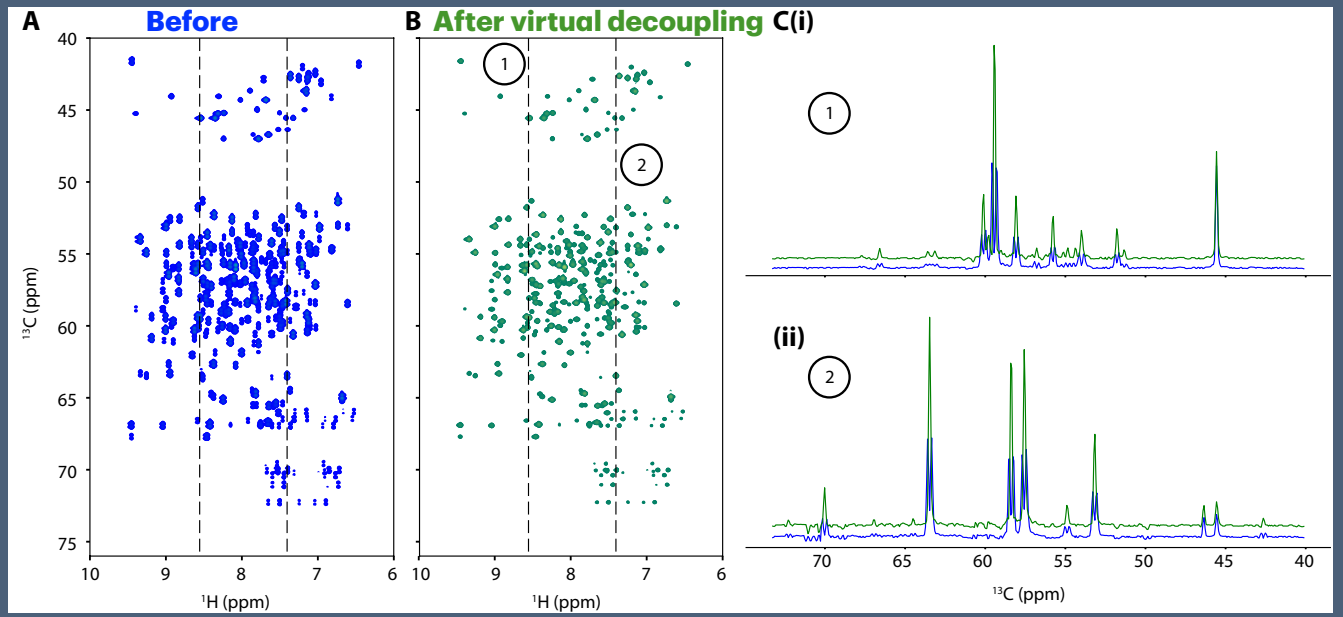


- 12.5% sampling
- 100 sampling schedule with a different Poisson-gap sampling schedule

Virtual Decoupling

$^{13}C_\alpha$-$^{13}C_\beta$ in 3D-HNCA and HN(CO)CA

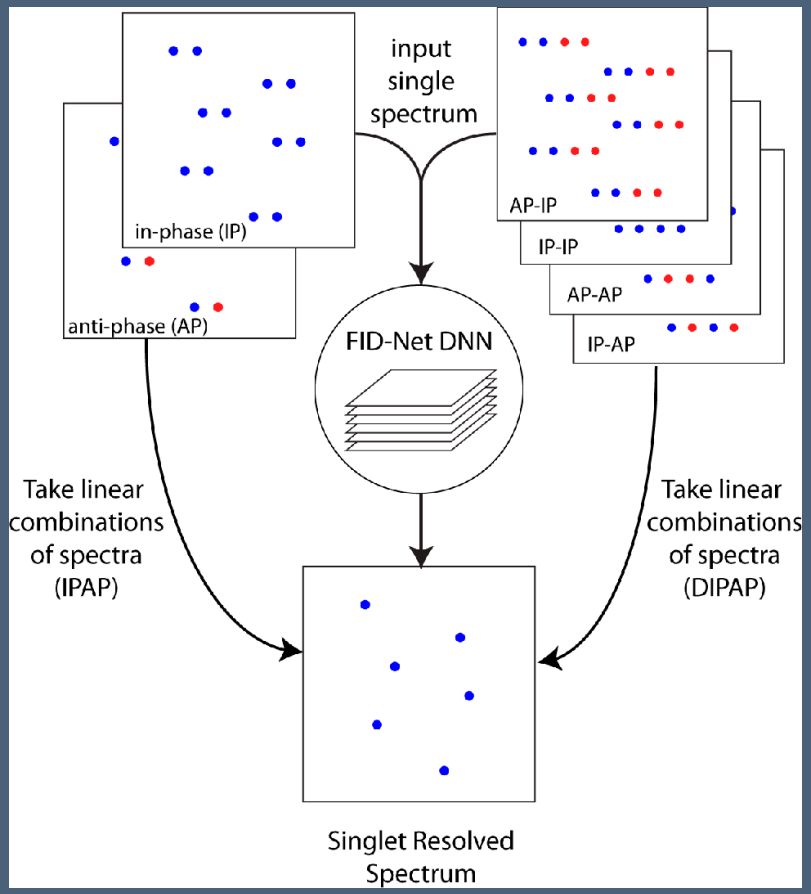




How successful doublets are successfully decoupled yielding an improvement in resolution and two-fold increase in sensitivity for these peaks while the singlet glycine peaks are unaltered

Virtual Decoupling (II)

^{13}C-^{13}C, ^{13}CO-^{15}N, $^{13}C_{\alpha}$-^{13}CO …

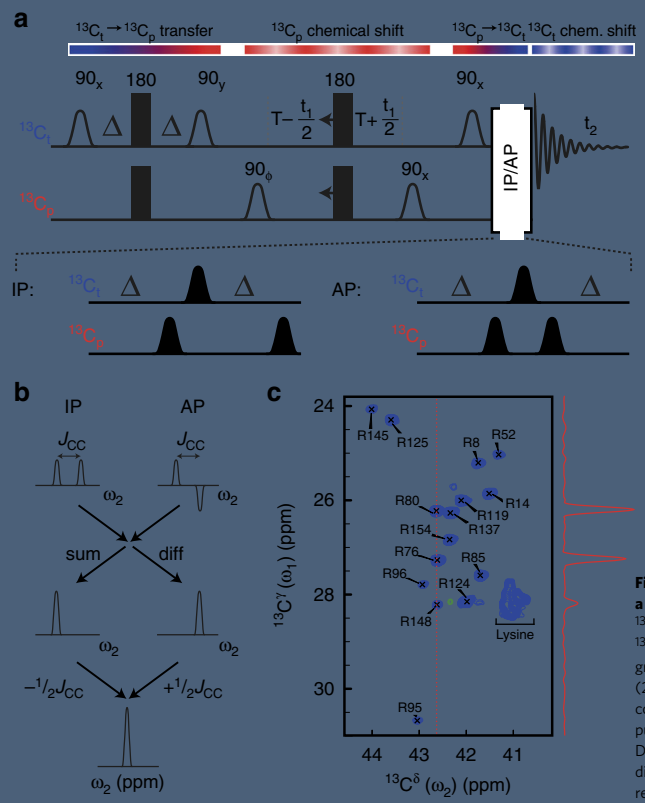


Traditional methods, such as IPAP and DIPAP, require the acquisition of multiple spectra and taking linear combinations to yield a singlet resolved spectrum.

Conversely, FID-Net-based DNNs can be trained to decouple spectra with one or two couplings using a single spectrum

Virtual Decoupling (III)

^{13}C-^{13}C side-chain correlation spectra for per-deuterated proteins



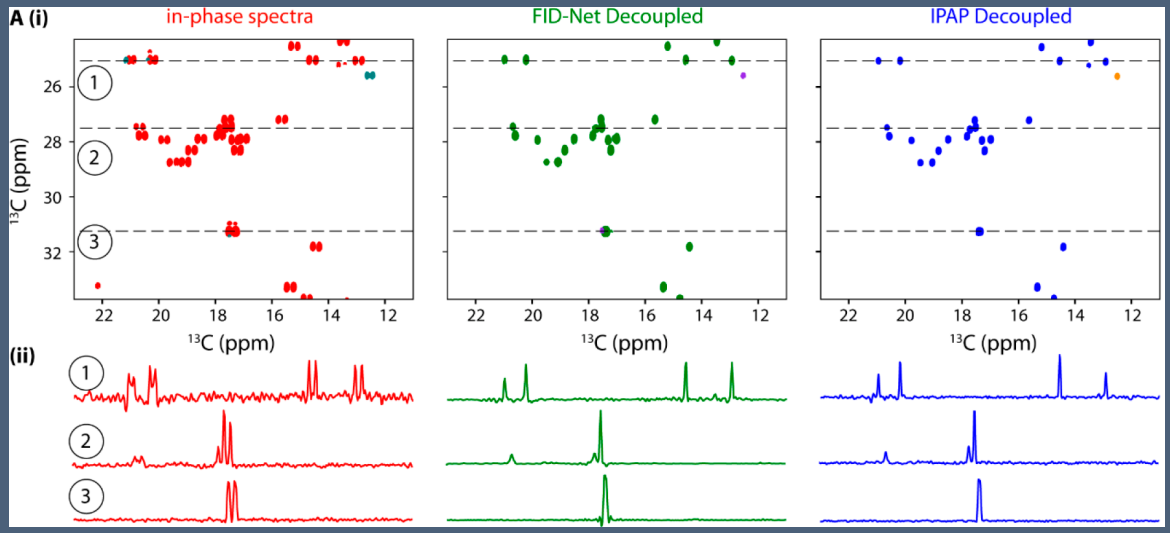
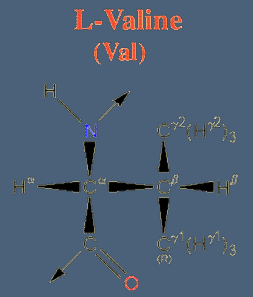


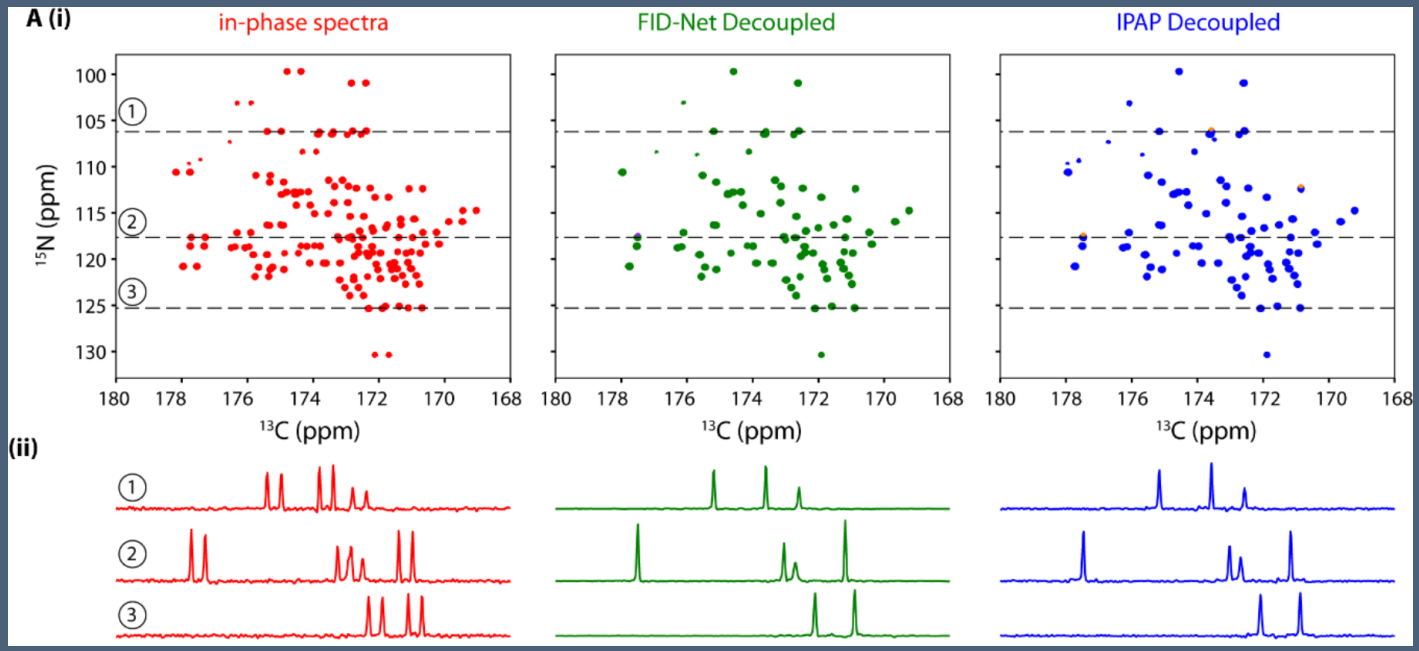
Fig. 2 ^{13}C-^{13}C side-chain correlation spectra of per-deuterated proteins. **a** Schematic representation of the NMR pulse sequence used to obtain ^{13}C–^{13}C side-chain correlation spectra. The flow of the magnetisation between $^{13}C_t$ (blue) and $^{13}C_p$ (red) is shown above the sequence with colour gradients. The following delays are used: $\Delta = 1/(4J_{CC}) \approx 7.1$ ms, $T = 1/(2J_{CC}) \approx 14.1$ ms, where J_{CC} is the one-bond ^{13}C–^{13}C scalar coupling constant. Rectangular pulses are high-power and not selective, bell-shaped pulses are frequency selective (90°: white outlined, 180°: black). Deuterium, ^2H, is decoupled throughout the sequence and frequency discrimination is obtained by states-TPPI of phase ϕ^{21}. **b** Schematic representation of post-processing to obtain the decoupled spectrum. **c** Arginine $^{13}C^\delta$–$^{13}C^\gamma$ correlation of the 18-kDa protein T4L L99A, obtained on a 1.4 mM sample at a static field of 14.1 T at 278 K in 37 min



Hansen DF, Nature Communications (2019) 10:1747 Hansen DF, JACS (2021) 143:16935-42

Virtual Decoupling (IV)

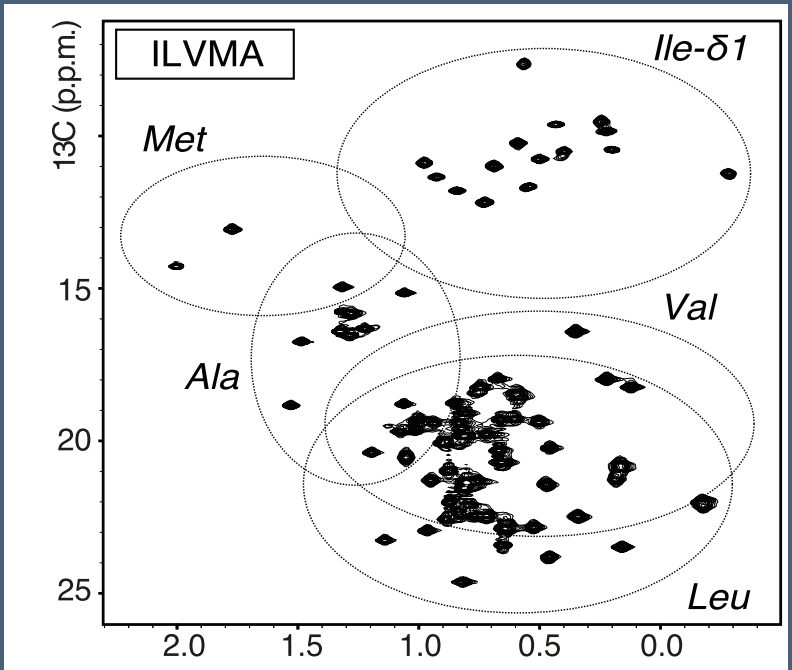
^{13}CO-^{15}N correlation spectra (CON)

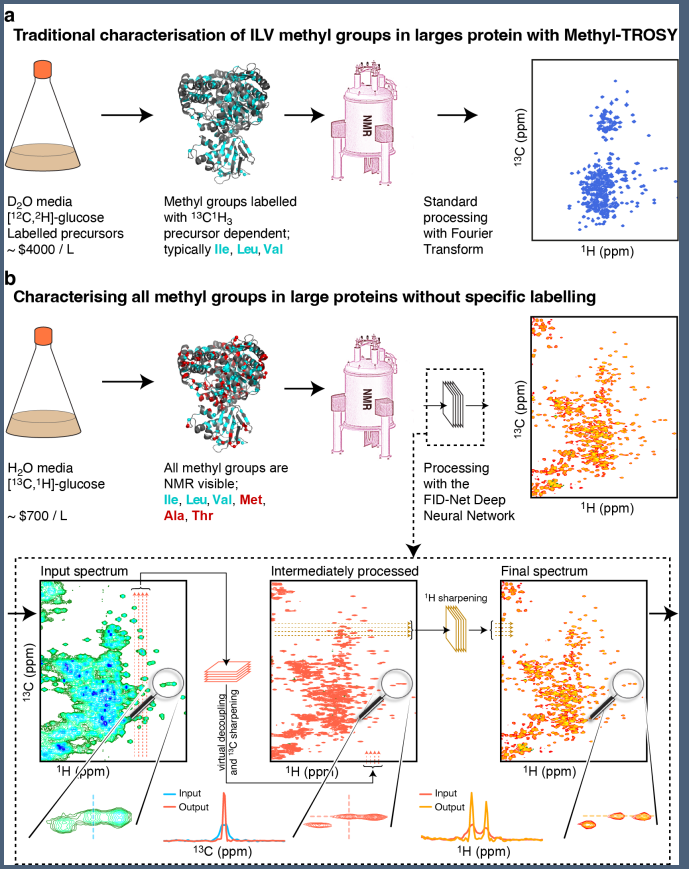


Hansen DF, JACS (2021) 143:16935-42

FID-Net on large protein systems

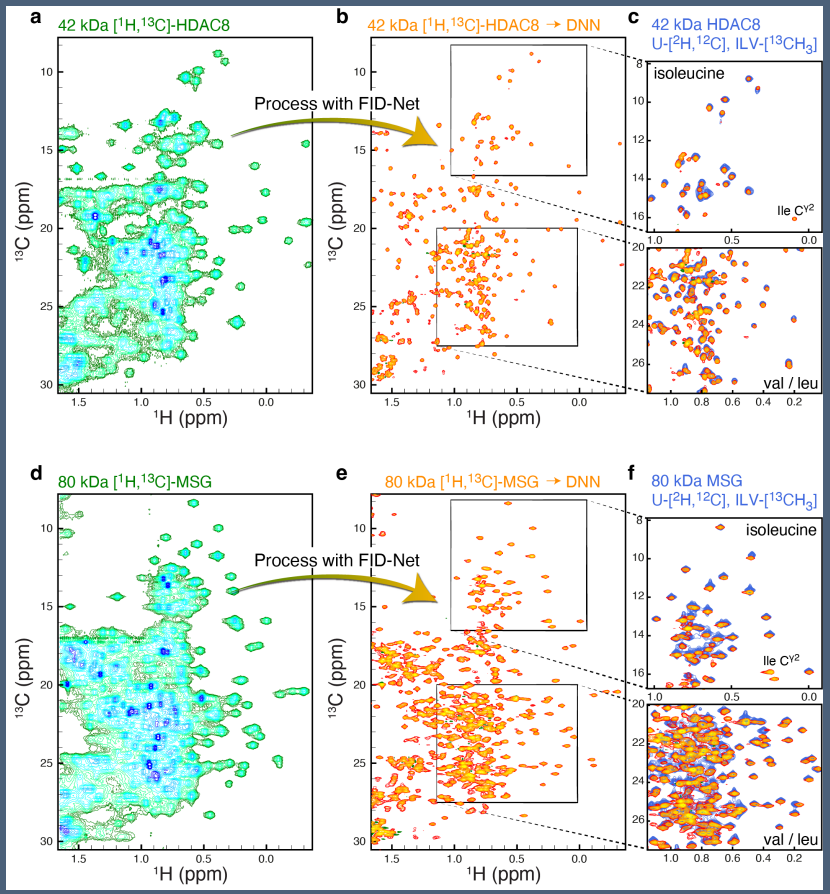
Methyl NMR Spectroscopy





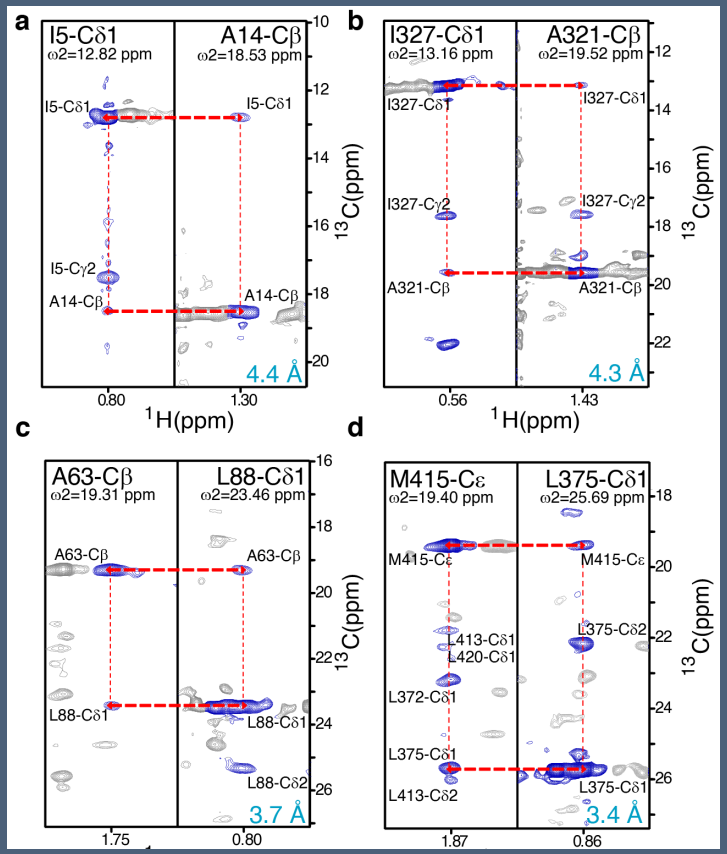
FID-Net on large protein systems

Methyl NMR Spectroscopy

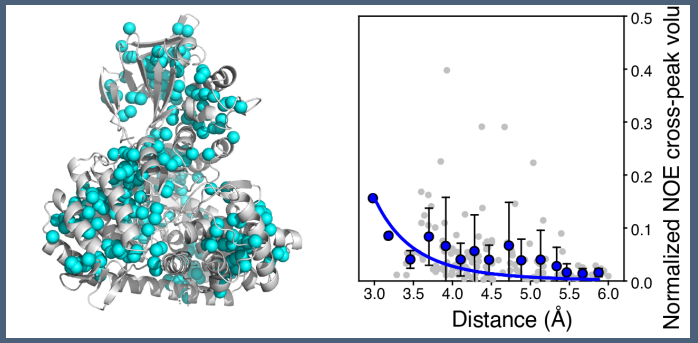


FID-Net on large protein systems

3D ^{13}C-HSQC-NOESY-HSQC non deuterated 80kDa MSG



312 NOE cross-peaks were observed among 170 methyl bearing residues from different regions of the protein



How to …

- https://github.com/gogulan-k/FID-Net
- d.hansen@ucl.ac.uk