

# WHY DO BIOLOGICAL NANOWIRES GLOW?

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## Introduction

The misfolding of proteins into insoluble amyloid fibril structures, that can aggregate within the brain, has been connected to neurodegenerative diseases. An intrinsic UV fluorescence from protein fibrils can be observed and is generated by electron delocalisation which is induced by aromatic amino acid side chains<sup>1</sup>. However, recently fluorescence in the visible range has been observed in protein amyloids lacking aromatic side chains<sup>2</sup>. This fluorescence has been connected to the fibrils cross- $\beta$  sheet structure which is stabilised by short, strong hydrogen bonds. Proton transfer across these hydrogen bonds creates a double-well ground state potential which engenders fluorescence<sup>3</sup>.

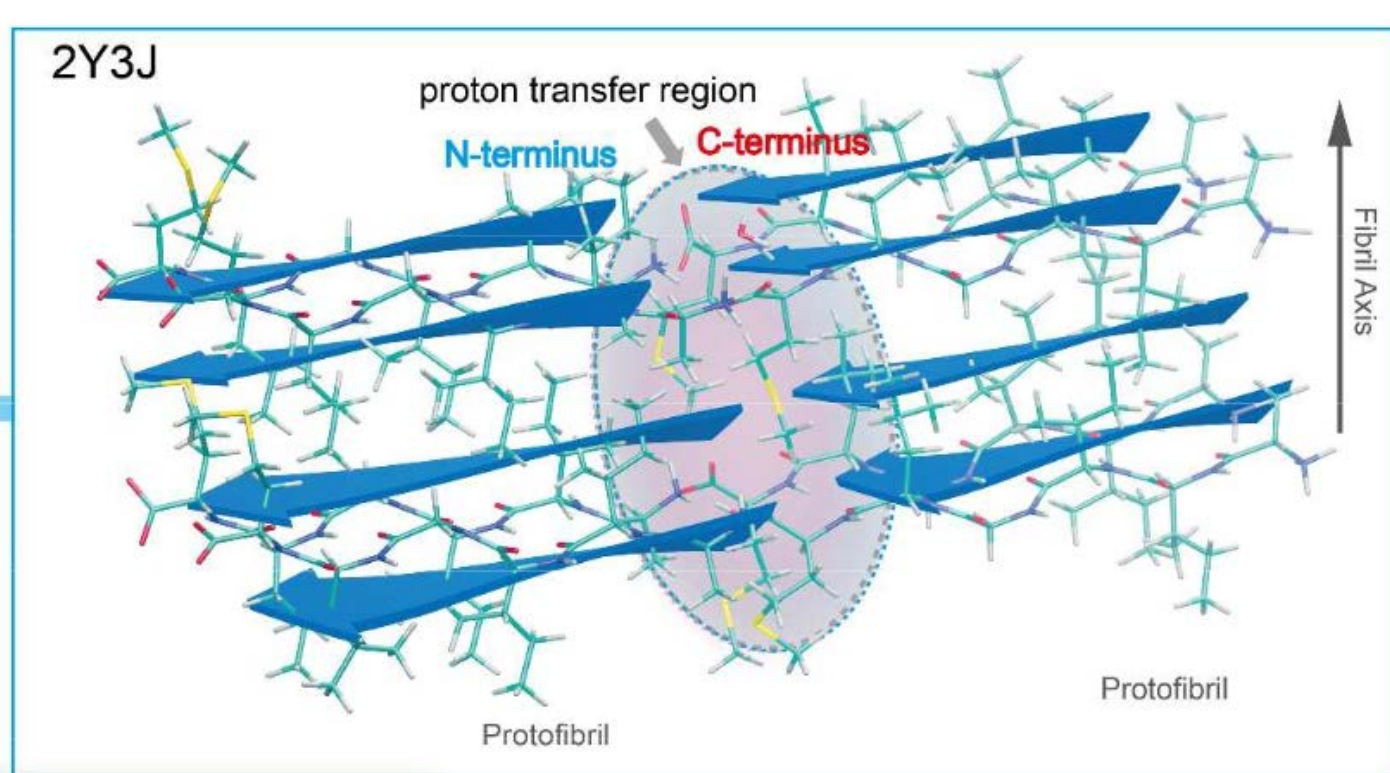


Figure 1: Cross- $\beta$  sheet structure and proton transfer region<sup>3</sup>.

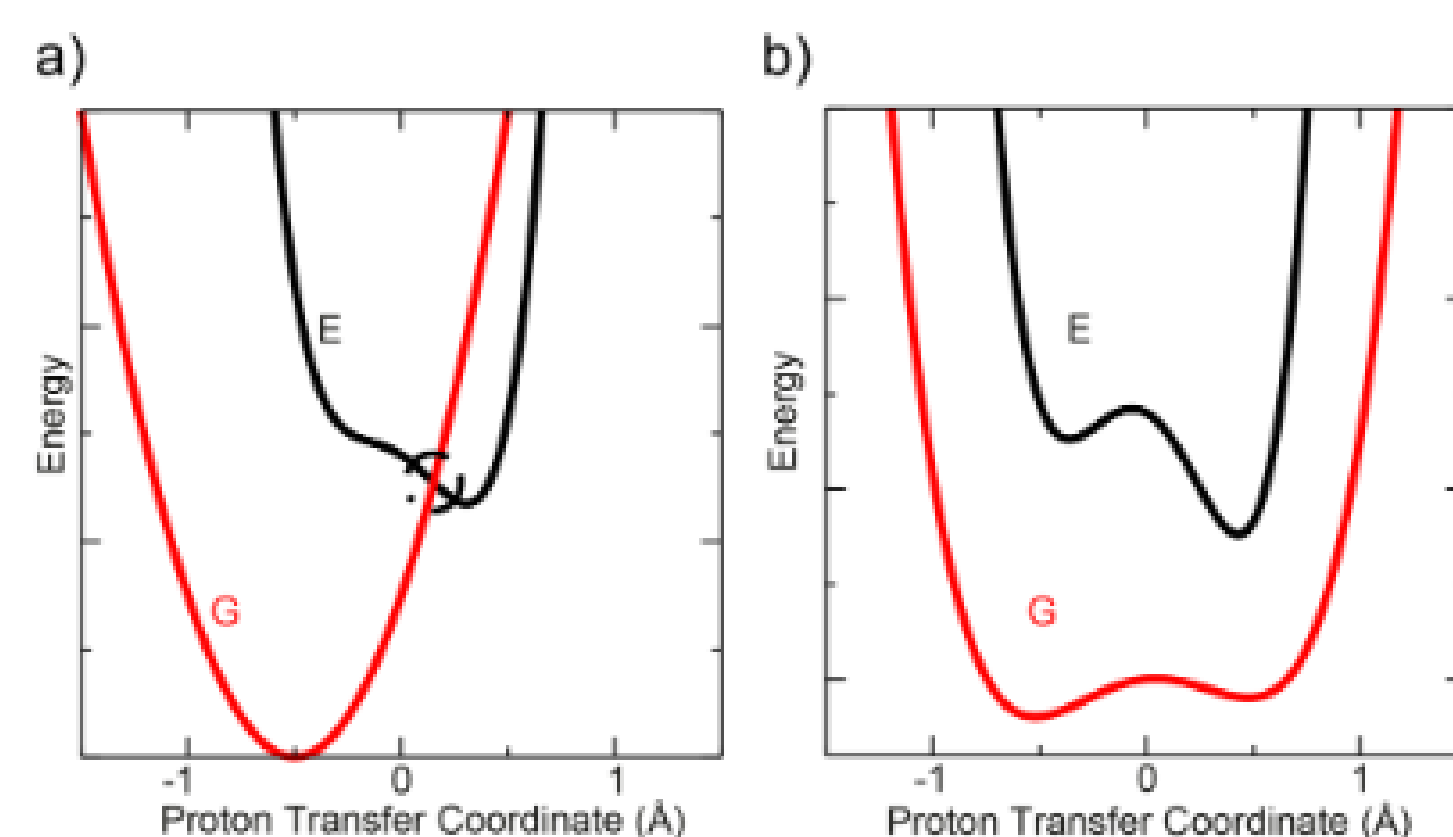


Figure 2: Single-well ground state potential (a). Double-well potential (b)<sup>3</sup>.

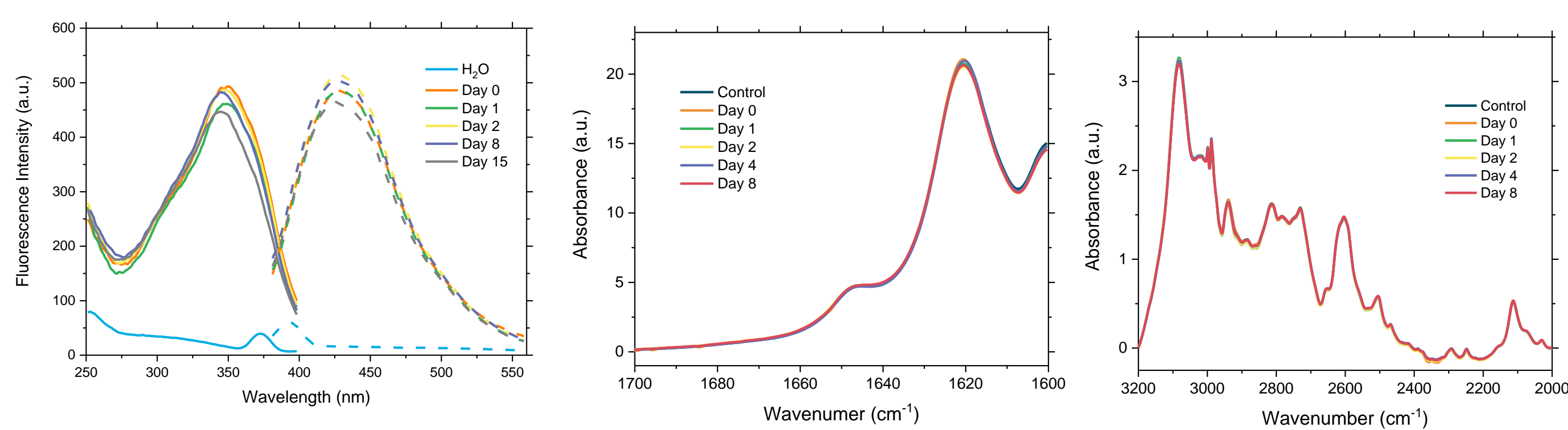
## Aims

- To determine if the three non-aromatic amino acids L-glutamine, L-alanine and L-lysine exhibit an intrinsic fluorescence.
- Use FTIR to structurally characterise the three amino acids and then explore the relationship between structure and the observed fluorescence.

## L-alanine and L-lysine

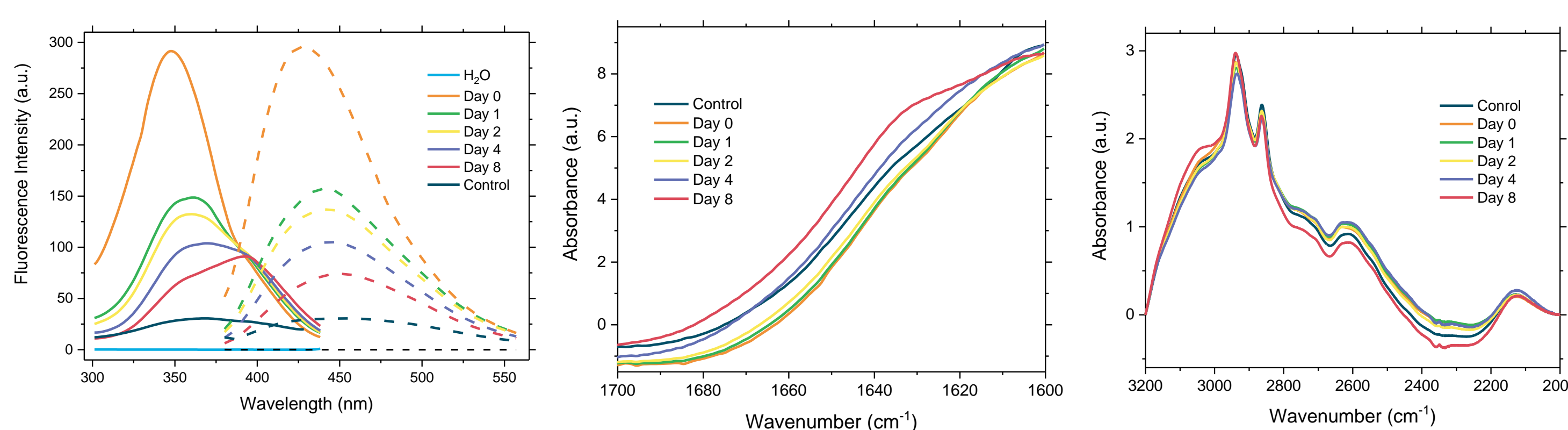
### L-alanine:

- Similar fluorescence to amyloid fibrils (left).
- Fluorescence is unchanging with time, with fluorescence observed from L-alanine in its as received powder form (i.e. naturally fluoresces).
- No evidence of structural change but suggests a  $\beta$ -sheet type structure (middle).
- No evidence of proton delocalisation (right).



### L-lysine:

- Similar fluorescence to amyloid fibrils with a decrease in fluorescence observed following incubation – very small natural fluorescence (left).
- No clear evidence of structural change (middle) or proton transfer (right).

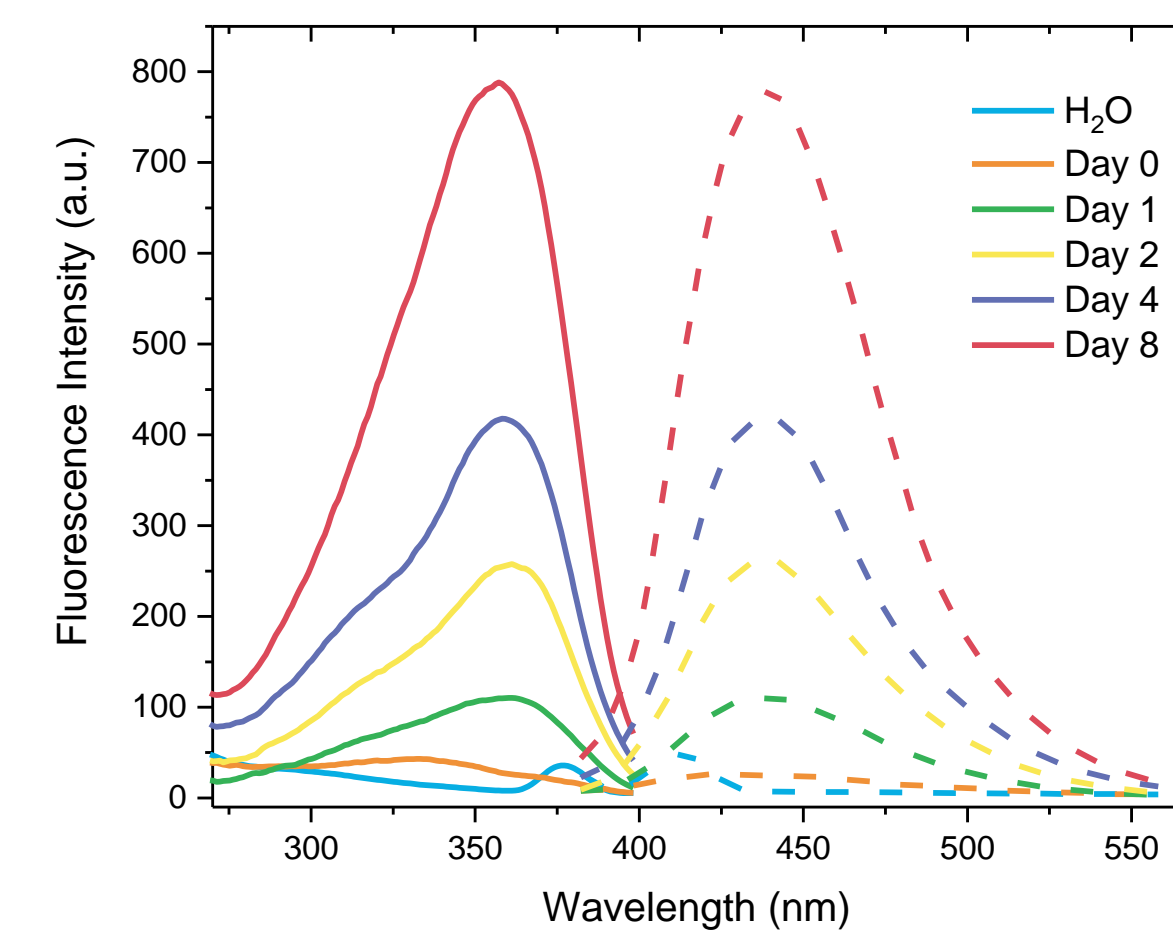
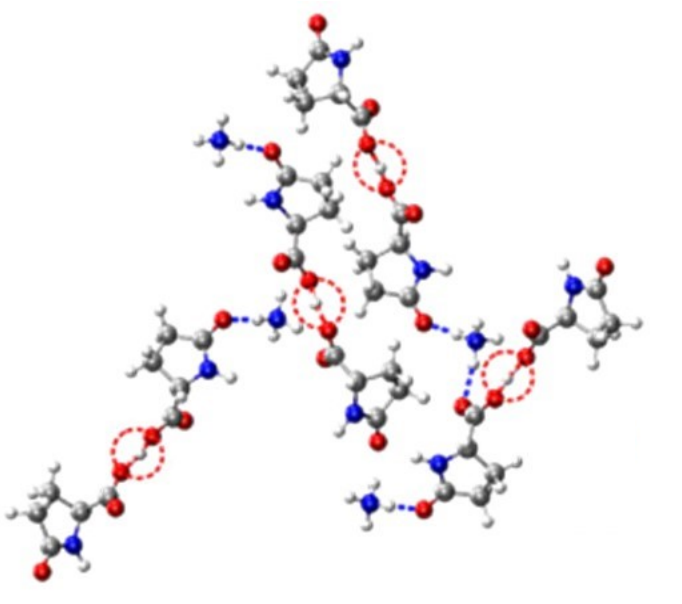


## References

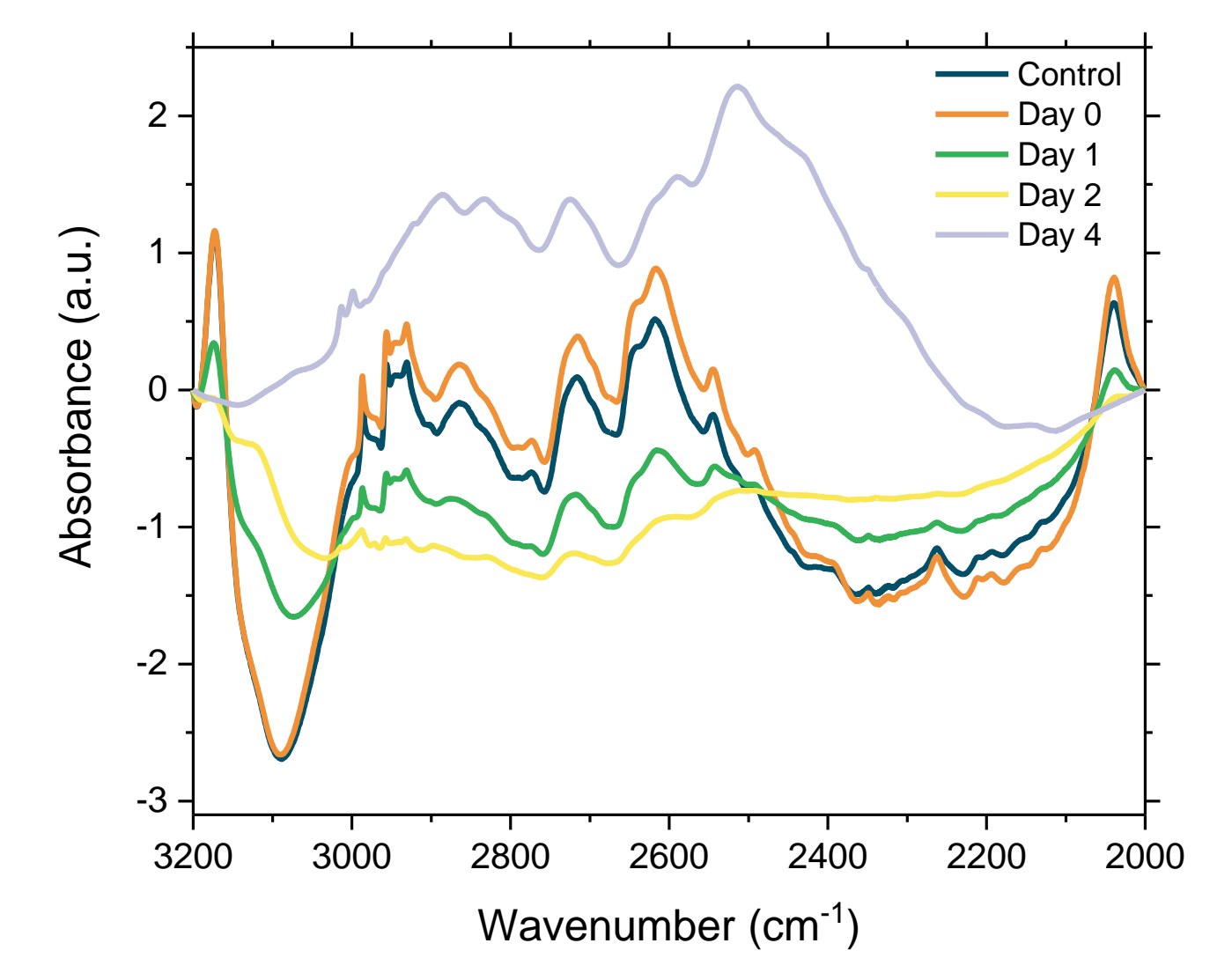
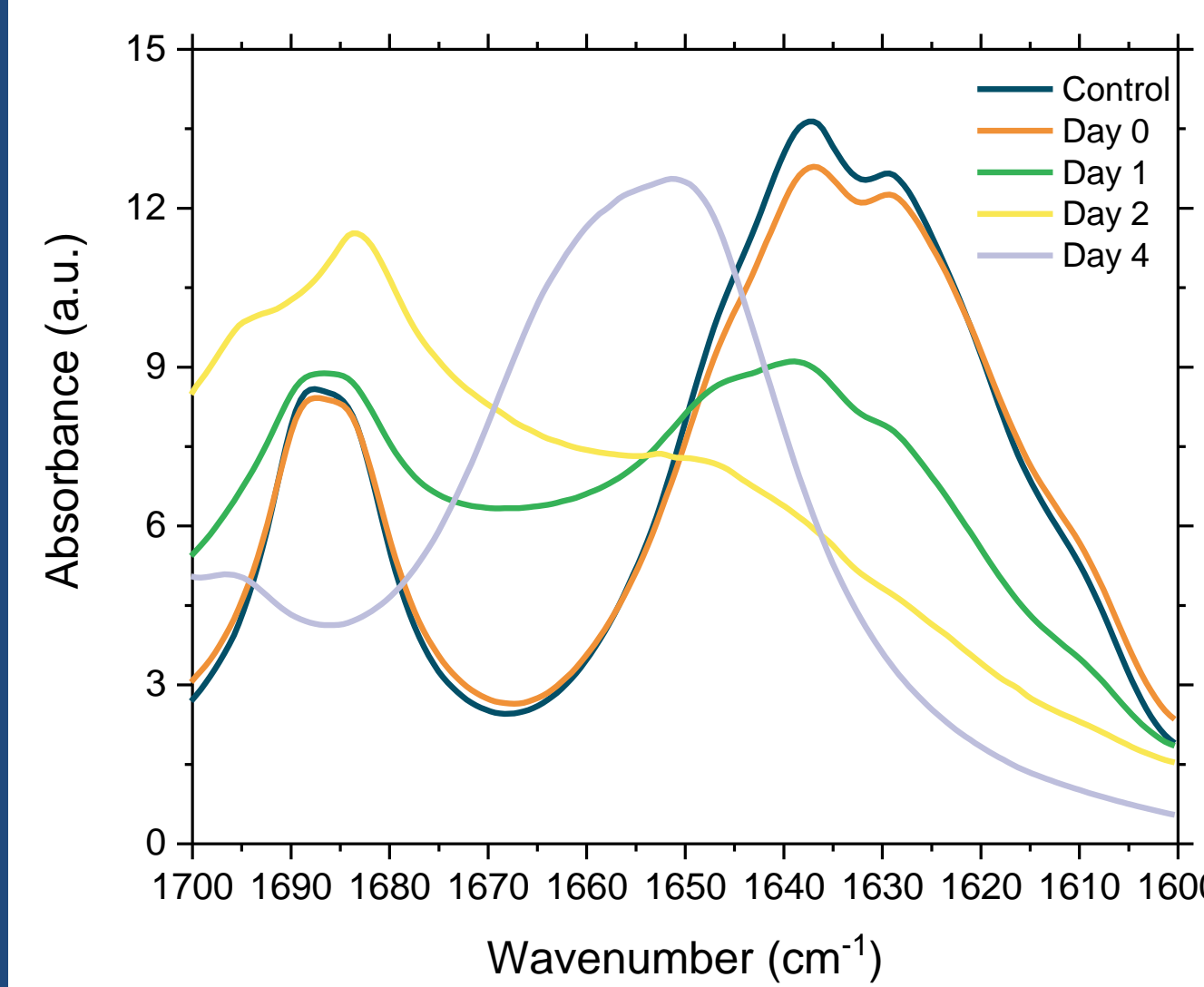
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## L-glutamine

XRD and THz-TDS has revealed that L-glutamine assembles into a structure that consists of short hydrogen bonds following incubation in water at 60°C. Molecular dynamic simulations indicate that the hydrogen bonds create a double-well ground state potential.



- A progressive increase in fluorescence was observed (following incubation) suggesting a structural change to a fibrillar like structure.
- Similar optical properties to amyloid proteins.
- No initial fluorescence was observed.



Evidence of structural change towards a  $\beta$ -turn type structure (left). Broadband shift of the peak provides evidence of proton transfer occurring (right) with the Day 4 shift up potentially providing evidence for protonation (as expected from simulations).

## Conclusion

All three amino acids displayed an intrinsic fluorescence in a similar visible region to amyloid proteins. The L-glutamine analysis connects an observed increase in fluorescence with structural changes, alongside an increase proton delocalisation. However, no structural change or proton delocalisation was definitively discernible for L-alanine or L-lysine, indicating that other mechanisms may give rise to fluorescence. Overall, although evidence seems to suggest that proton delocalisation and structure plays a role in the observed fluorescence (with short hydrogen bonds connecting these characteristics), the difference in optical properties observed between the three amino acids signifies that the fundamental mechanism through which the observed fluorescence arises is yet to be fully understood. Sensors that detect the fluorescence could be developed to investigate the formation and aggregation of protein fibrils both in vitro and in vivo, helping to discern how neurodegenerative diseases develop, whilst assisting in the development of amyloidogenesis inhibitors<sup>4</sup>.

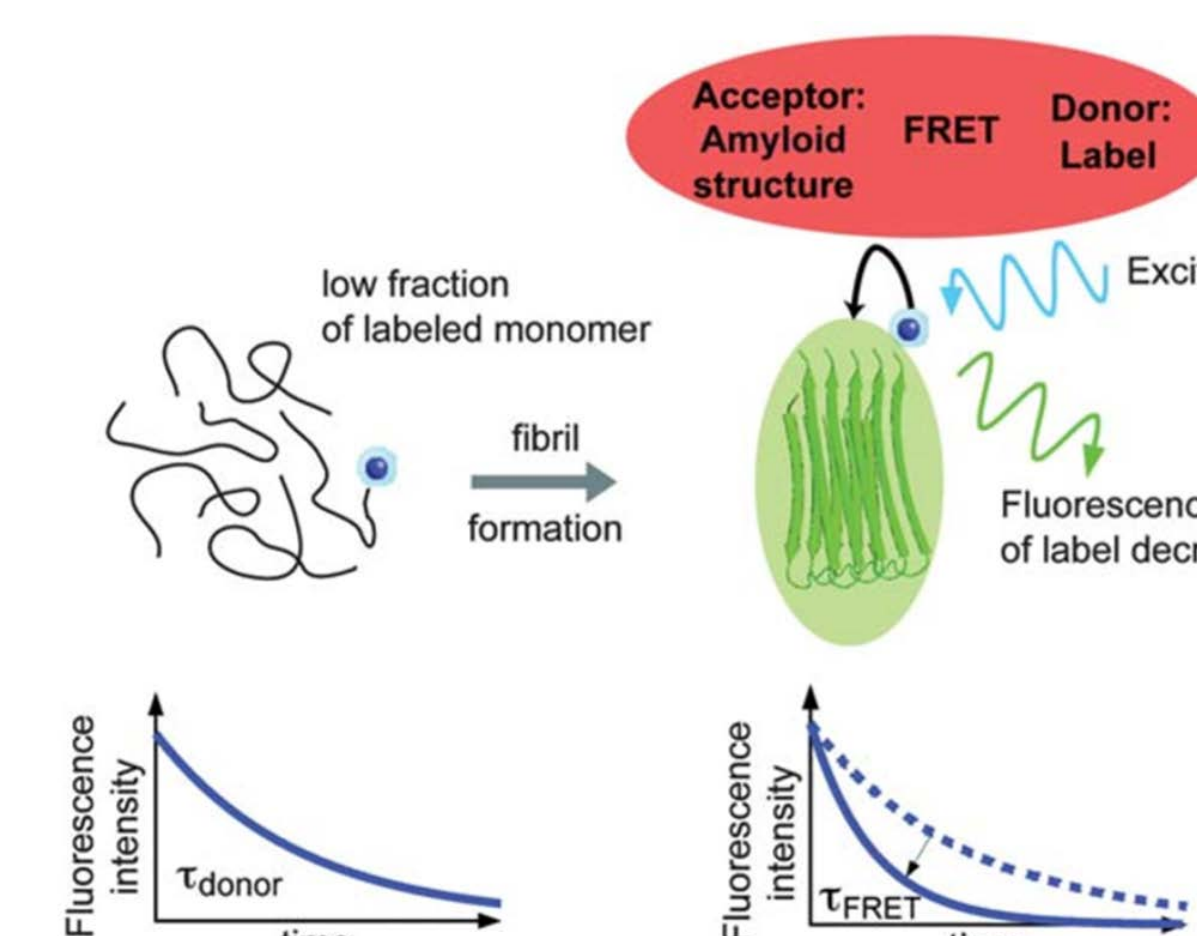


Figure 3: In vivo sensing of amyloid formation utilising FRET<sup>3</sup>.

## Acknowledgments

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