Probing Methionine Uptake in Live Cells and Tissue by Deuterium Labelling and Stimulated Raman Scattering

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The small biomolecule methionine (Met) is a fundamental amino acid required for a vast range of biological processes such as protein synthesis, cancer metabolism, and epigenetics. However, it is difficult to visualize the subcellular distribution of small biomolecules including Met in a minimally invasive manner. Recently, we demonstrated stimulated Raman scattering (SRS) imaging [1] of cellular uptake of deuterated methionine (d_8-Met) in live HeLa cells [2]. By careful image analysis with background subtraction, we succeeded in the SRS imaging of cellular uptake of d_8-Met with a much greater signal intensity than homopropargylglycine (Hpg), the previously used alkyne-labeled Met analogue, even though their solutions show similar SRS signal intensities. We took this as a possible reflection of the increased and minimally invasive uptake kinetics of d_8-Met compared with Hpg. Here, we expand further upon this method introducing investigations in live tissue from the fruit fly *Drosophila melanogaster*. We show that d_8-Met is incorporated into tissue systemically from simply feeding larvae and thus paving the way for studies of cells and tissue from *Drosophila*. We anticipate that d_8-Met and other deuterated biomolecules will be useful for investigating metabolic processes with subcellular resolution.

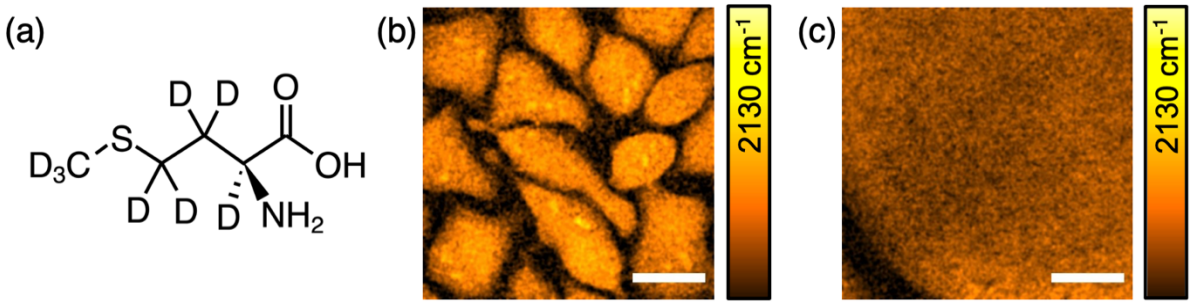

Fig. 1. Long-term metabolic profiling by stimulated Raman scattering. (a) Molecular structure of deuterated methionine (d_8-Met). (b, c) SRS images - HeLa cells (b) cultured in the presence of d_8-Met after 5-days incubation, - *Drosophila* imaginal wing disc (c) dissected from a wandering 3rd instar larva after 2-days of feeding on d_8-Met supplemented food. Scale bars, 20 μm.

References

[1] J. -X. Cheng, W. Min, Y. Ozeki, D. Polli, 'Stimulated Raman scattering microscopy -Techniques and Applications-,' Elsevier, 2021.

[2] S. J. Spratt *et al.*, J. Phys. Chem. B **126**, 1633 (2022).