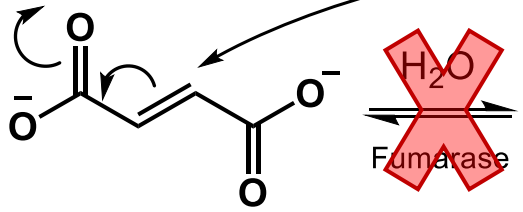
May post-translational succination be involved in cardiac arrhythmia?

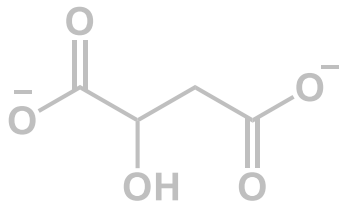
A joint experimental and theoretical study combining CIU and molecular dynamics approaches

L. Groignet, D. Dellemme, J.-M. Colet, M. Surin, P. Brocorens, J. De Winter, *University of Mons*

During Krebs cycle :

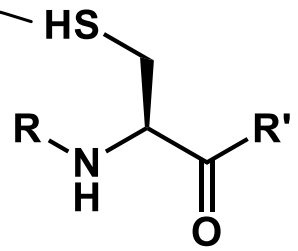


Fumarate



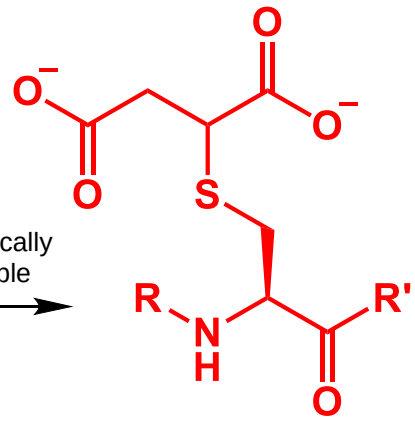
Malate

Succination reaction:



Cysteine

Physiologically irreversible

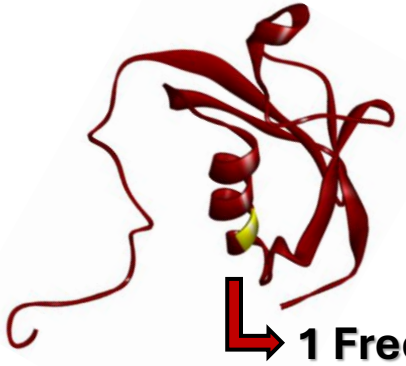


2-succinyl cysteine

→ In some diseases : underexpression of fumarase → **Accumulation of Fumarate**

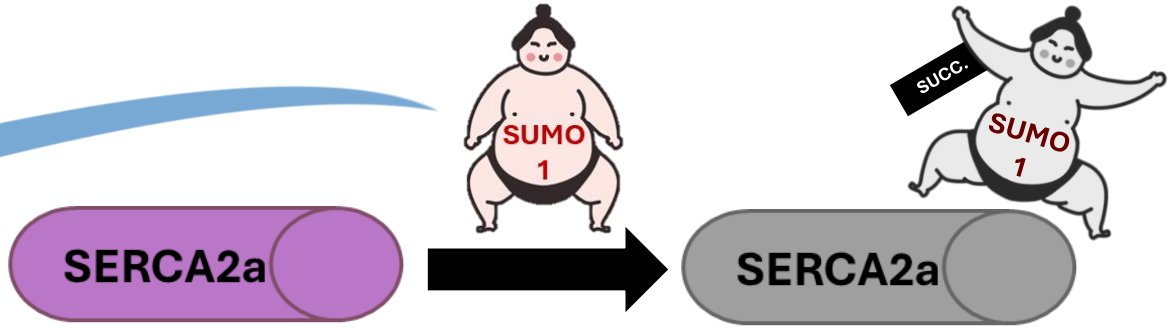
→ Michael additions between thiol functions (cysteines) and fumarate = **SUCCINATION**

In heart cells



1 Free Cys

Small Ubiquitin like MOdifier 1 (SUMO1)



Why ?
- Activity (Ca^{2+} pump)
- **Stability**
- Etc.

Does succination destabilize 3D' structure of SUMO1 ?

↓

Affects the interaction between SUMO1/SERCA2a ?

↓

Is succination involved in cardiac arrhythmia ?

May post-translational succination be involved in cardiac arrhythmia?

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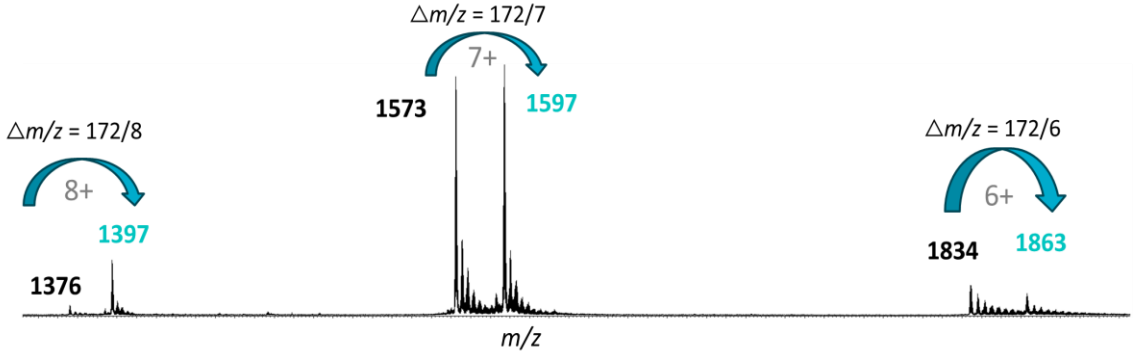
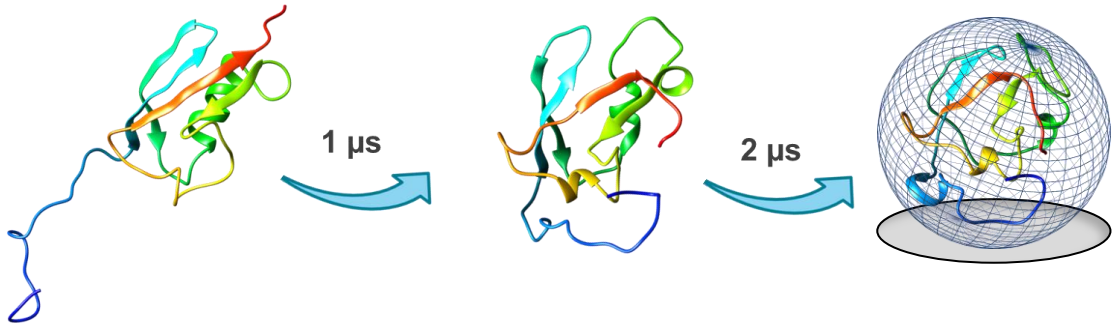
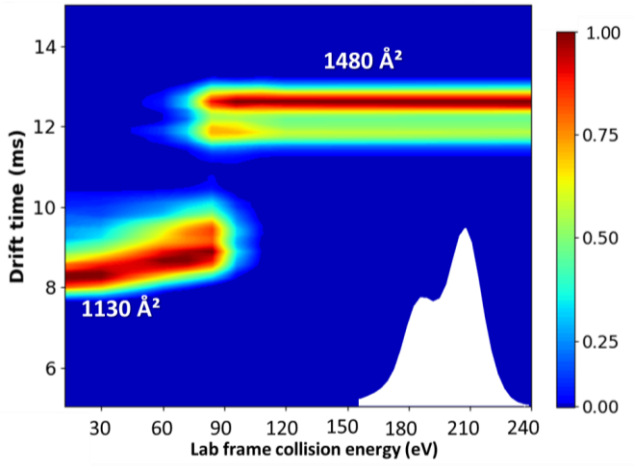
How to evaluate the 3D' structure of SUMO1 before/after succination ?

Experimentally : (Ion Mobility) Mass Spectrometry ⟺ Theoretically : Molecular dynamics







→ Succination's spontaneity
→ Collisional cross section
→ Collision Induced Unfolding
→ Etc.

If you want to discuss : **P65**
Thank you for your attention !

S²MOs

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CMN