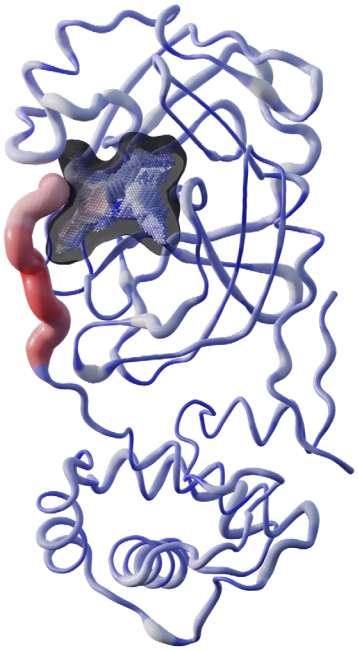
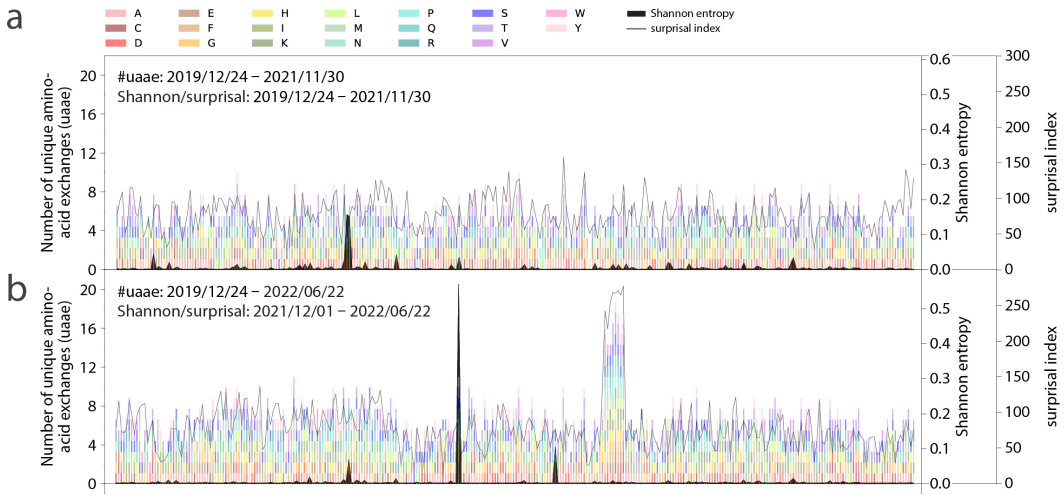


Structural representation of mutation dynamics showing unique amino-acid exchanges along the protein sequence, , including genomes sampled until June 2022. Thickness of the ribbon corresponds to number of mutations present at given position.

CASE STUDY | DISEASE MONITORING

Tracking **Mutational Dynamics**

Therapeutic options such as SARS-CoV-2 main-protease (M^{pro}) inhibitors are essential due to the ongoing evolution toward escape from natural or induced immunity. Although mutation rates are considered moderate to high in coronaviruses, as observed in recent years with the spike protein, the mutational dynamics of M^{pro} have generally been considered negligible. Analyses of recent SARS-CoV-2 genomic data suggested accelerated mutational dynamics near the active site of M^{pro} since early December 2021. Our findings emphasise the importance of monitoring the mutational dynamics of M^{pro} and the potential consequences of arising amino-acid exchanges in regions critial for the susceptibility of the virus to antivirals targeting the protease.



Mutation dynamics in the M^{pro} amino-acid sequence.

a: Final distribution of unique amino-acid exchanges for every position within the wild-type M^{pro} sequence. Collection date before December 2021 (transparent multi-colored bars). Associated surprisal indices and Shannon entropies are superimposed in light and dark gray, respectively. **b**: As in a, collection dates up until June 22nd 2022, with associated surprisal indices and Shannon entropies calculated from sequences collected from December 1st 2021 to June 22nd 2022.

L. Parigger, A. Krassnigg, T. Schopper, A. Singh, K. Tappler, K. Köchl, M. Hetmann, K. Gruber, G. Steinkellner and C. C. Gruber *Front. Med.* 2022, **9**:1061142. doi: 10.3389/fmed.2022.1061142.