

**Experiment title: Fusion domain of the spike protein of Mouse Hepatitis Virus**

(Data collected as part of the BAG CNRS -Gif sur Yvette coordinated by M. Knossow)

Experiment number:
LS 1798

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Report: Coronaviruses are large, enveloped, plus-strand RNA viruses. They cause highly prevalent diseases in humans and domestic animals and include human respiratory coronavirus (the "common cold" virus) and feline infectious peritonitis virus, among others. They cause systemic or localized infections, depending on whether or not they are restricted to a few cell types. Host specificity and membrane fusion are mediated by the spike glycoprotein, S. Mouse hepatitis virus (MHV) has been the object of intense study as a convenient model for coronaviruses. An accurate structure of the fusion domain of MHV-S could prove an important insight into the virus-cell interactions. On the practical side, it could lead to the design of antiviral drugs that interfere with the function of the spike protein. Indeed, it is known that virus infectivity can be neutralized by inhibition of membrane fusion (e.g., with monoclonal anti-S antibodies).

The complete S protein is a membrane protein of some 1600 residues. Of those, residues 953-1048 and 1216-1254 form the membrane fusion domain. This domain was reconstituted by producing the two polypeptides in *E. coli* and assembling them *in vitro*. They form a highly stable heterodimer that was crystallised both in the native form and as a selenomethionine derivative.

We collected a native dataset on this project. The crystals belong to spacegroup R32 with cell parameters $a=b=55 \text{ \AA}$, $c=298 \text{ \AA}$, $\alpha=\beta=90^\circ$, $\gamma=120^\circ$. Diffraction is anisotropic, extending beyond 2 \AA along c^* and to about 2.7 \AA along a^* , b^* . R_{sym} is 4.6% by taking all reflections between 20 and 2.4 \AA (completeness 99.7%, multiplicity 5.5). This

dataset will be used for refinement once we get a starting model from the selenomethionine derivative.