

Figures for Feasibility and Data:

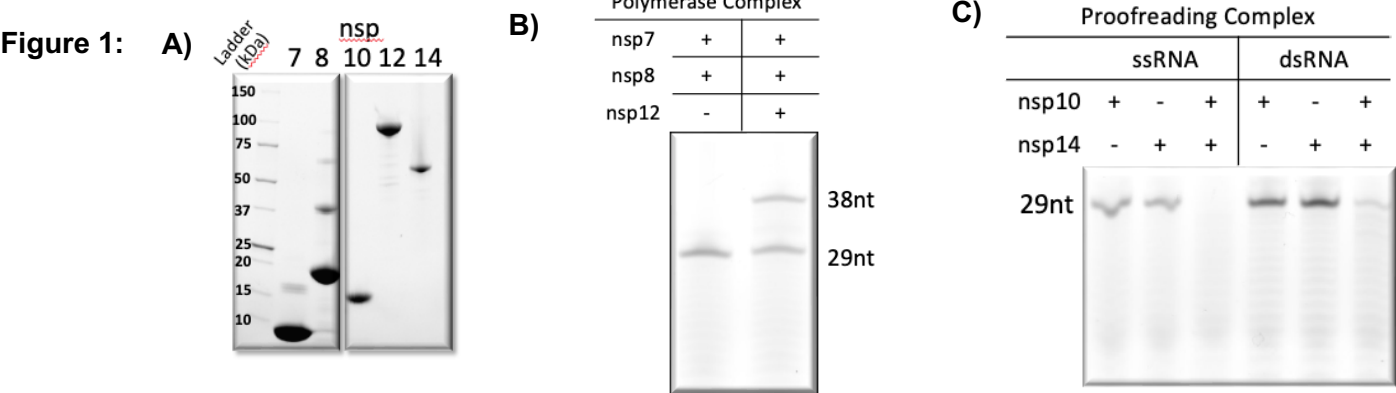


Figure 1: Active SARS-CoV-2 polymerase and proofreading complexes. **A)** Expression and purification of SARS-CoV-2 non-structural proteins: *nsp7* (9kDa), *nsp8* (22kDa), *nsp10* (15kDa), *nsp14* (60kDa), *nsp12* (110kDa). **B)** The *nsp12* polymerase extends RNA primers (29nt) in the presence of *nsp7* and *nsp8* to a full length product (38nt). **C)** The proofreading complex degrades both single and double-stranded RNA. The proofreading complex is of 3'-5' exonuclease *nsp14* and cofactor *nsp10*.

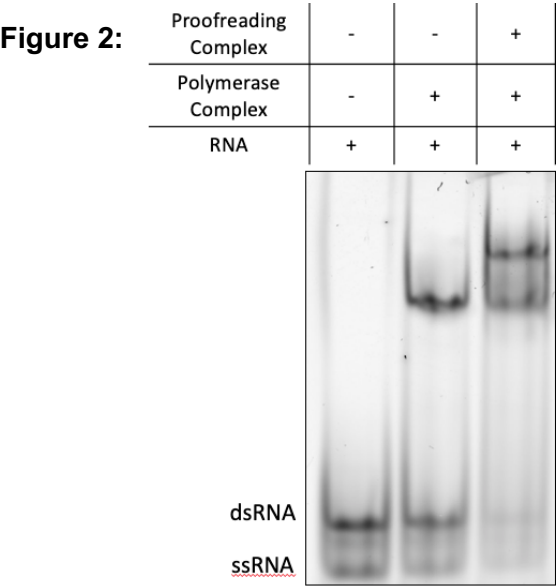


Figure 2: Assembly of a polymerase + proofreading complex. Primer-template pairs labeled with a fluorophore bind the polymerase complex causing a reduced gel mobility by native-PAGE. Addition of the proofreading complex results in a further shift. Complex formation of the RNA+polymerase is indicated by the number 1, while formation of a RNA+polymerase+proofreading complex is indicated by the number 2.

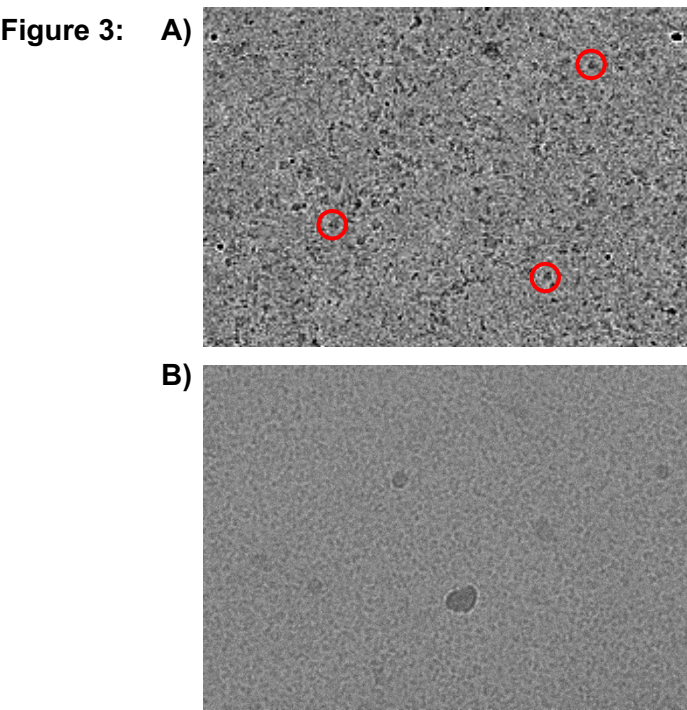


Figure 3: Disassembly of polymerase+proofreading complexes during blot-plunge vitrification. Samples of either coronavirus polymerase (A) or polymerase+proofreading (B) complexes prepared at 1mg/mL, frozen using blot-plunge vitrification and imaged using a 200kV Talos Arctica cryo-electron microscope under similar protocols. Polymerase complexes present as defined puncta in the EM images (red circles) and allow the determination of high-resolution structures. Polymerase+proofreading complexes display as ill-defined and likely disassembled complexes and/or denatured proteins.