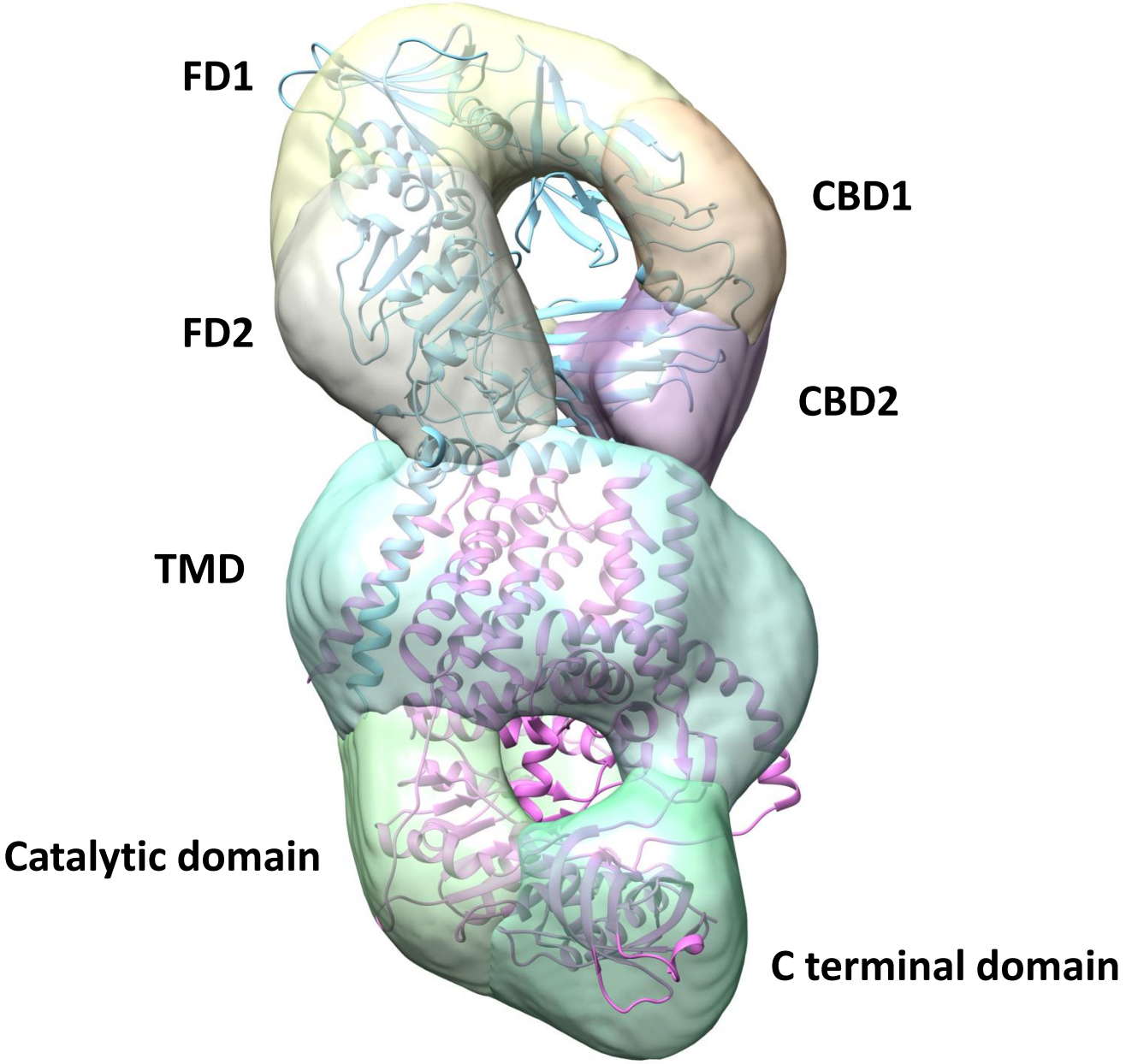S6 Fig