

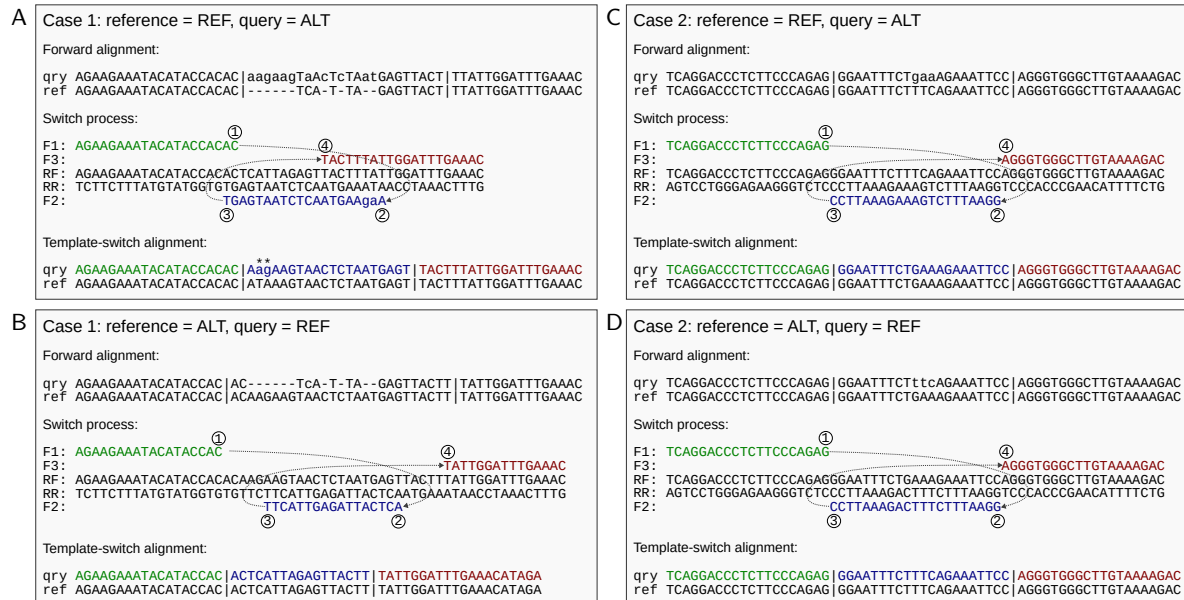


Fig S4. Direction of TSMs. **(A)** The complex mutation (top) is partially explained by the TSM mechanism when the REF allele is used as the reference (middle); the solution (bottom) contains two mismatches (marked with asterisks). **(B)** With the ALT allele as the reference, the complex mutation is fully explained, indicating that ALT is the ancestral state and REF is a derived state. **(C,D)** The inversions in place cannot be polarised as both arrangements fully explain the complex mutation pattern with a single TSM event.