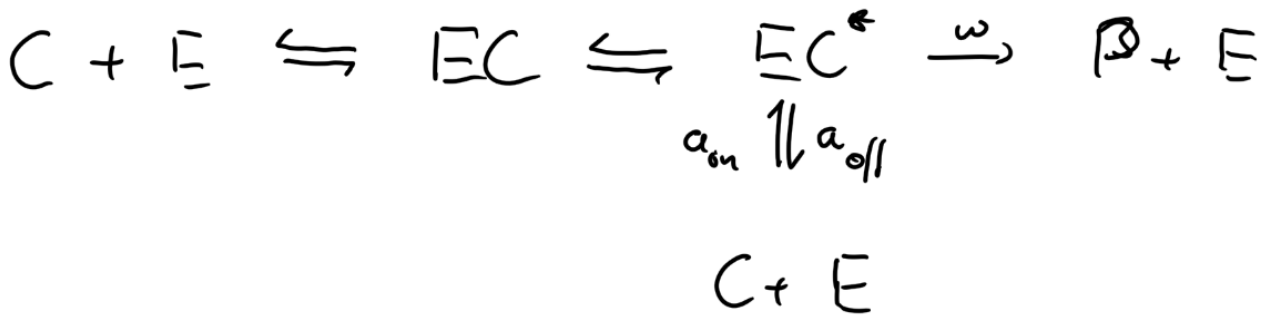
Kinetic Proofreading

Non-equilibrium transitions are required to increase accuracy beyond the limit from the energy of discrimination. Independently discovered by Hopfield and Ninio

- JJ Hopfield (October 1974). "Kinetic proofreading: a new mechanism for reducing errors in biosynthetic processes requiring high specificity". Proc. Natl. Acad. Sci. U.S.A. 71
- Ninio J (1975). "Kinetic amplification of enzyme discrimination". Biochimie. 57 (5): 587–95.

Increasing accuracy through intermediate states

Let's consider how an intermediate state EC^* changes this situation:



In this reaction, there is a reversible step from EC to EC' without any additional input of energy such that at equilibrium the state EC^* is going to be populated according to Boltzmann statistics. The analogous equation can be written down for the wrong substrate C' and the corresponding transition state will again be Boltzmann populated. Hence **nothing is gained**.

Increasing accuracy requires non-equilibrium steps

Now consider the case where the EC to EC^* step is coupled to ATP hydrolysis:

- no alternative path into EC^* (a_{on} is very small)
- populations of EC^* can differ from Boltzmann statistics
- continued decay of EC'^* can enrich for the correct EC^*

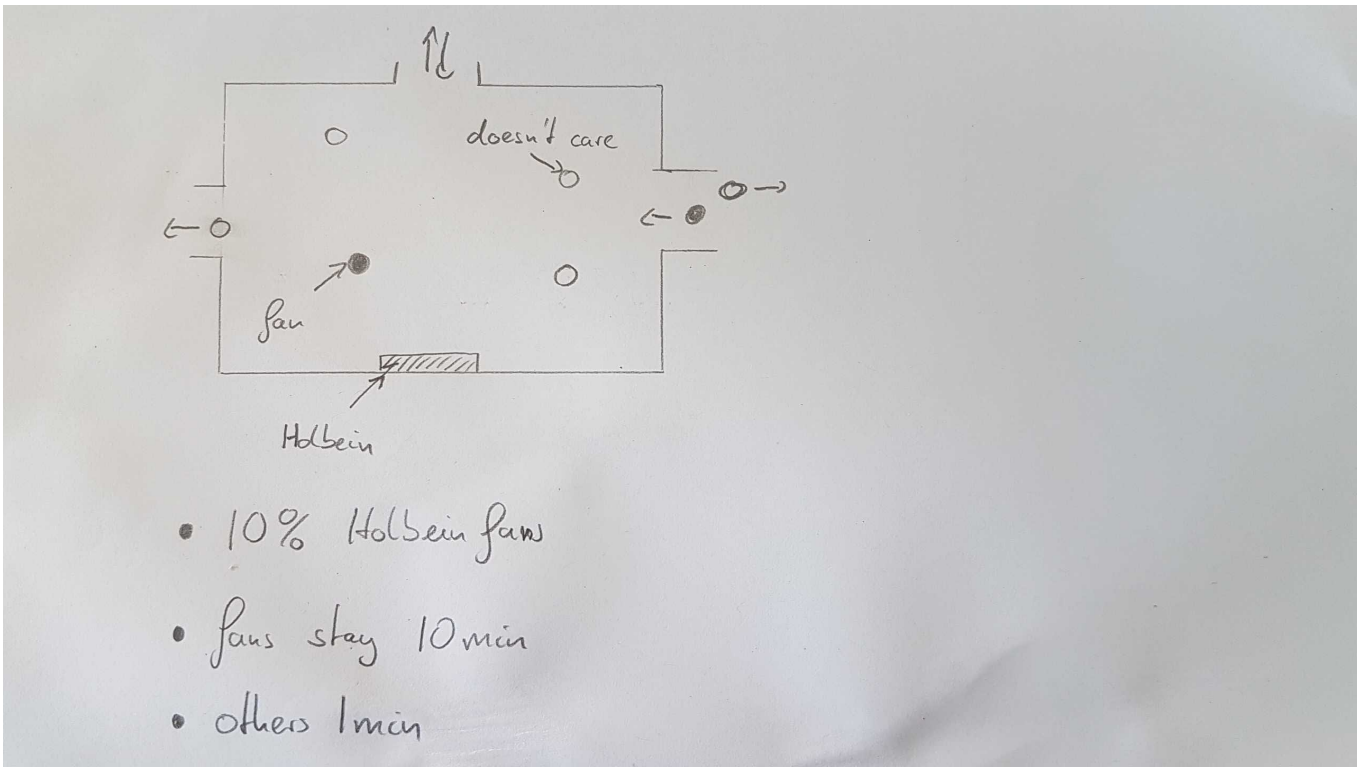
Proofreading is ubiquitous

- Energy consuming proof-reading steps are very common
- Often involve conformational transitions or modification
- Not only important for biochemistry, but also sensing.

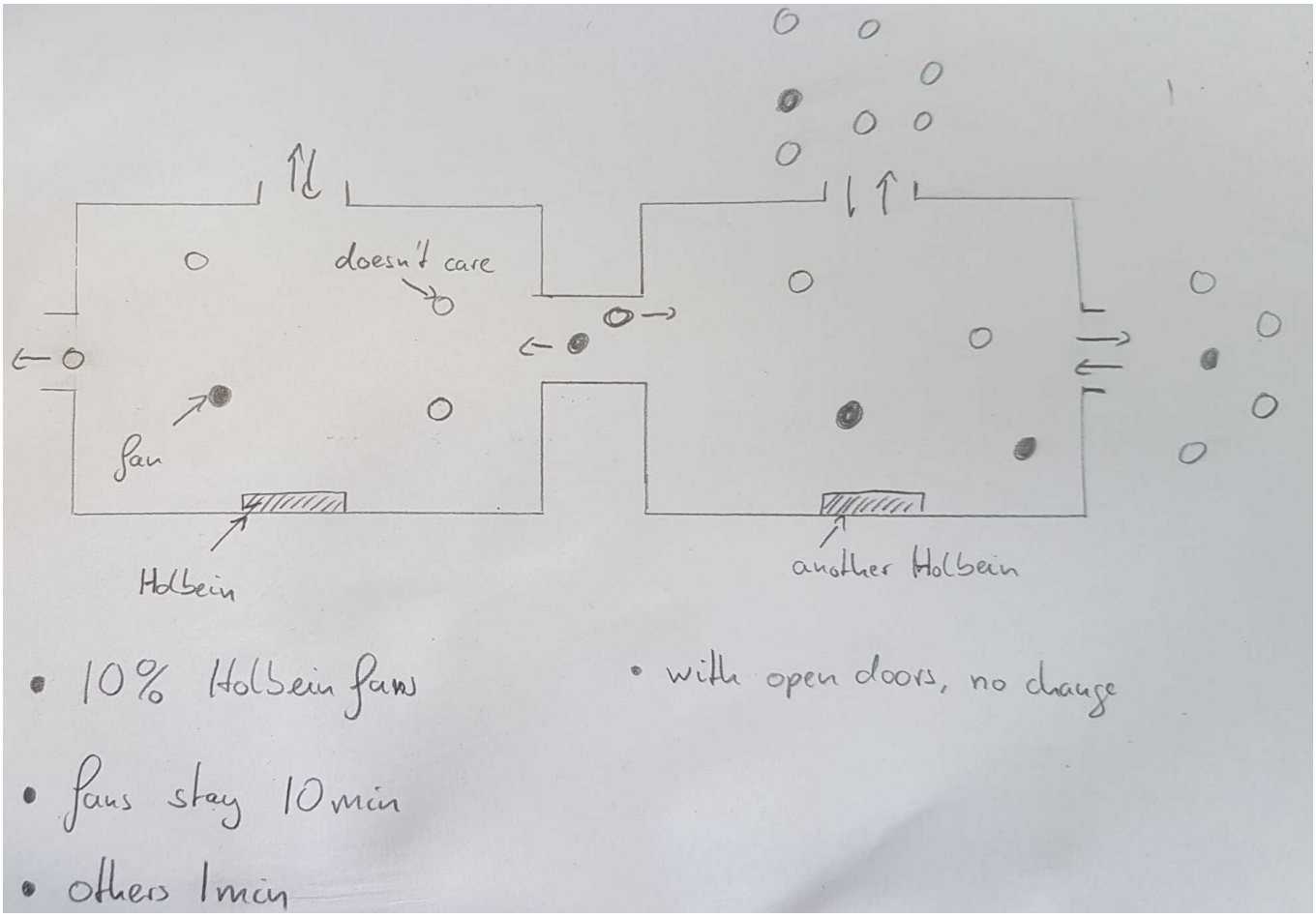
Intuitive example of the core idea of kinetic proof-reading

This is a somewhat tongue-in-cheek illustration on how kinetic proof-reading works and why non-reversibility is important. Going through this hopefully helps you to understand the core of the paper better. It is inspired by similar examples on the internet... I didn't come up with this.

How do you tell fans of Holbein in a museum form non-fans?



Adding a second picture in a neighboring room doesn't help much!



One-way doors!