RecurPocket: Recurrent Lmser Network with Gating Mechanism for Protein Binding Site Detection

I. APPENDIX

A. On Kalasanty settings [1]

Kalasanty network is based on U-Net with forward skip connections. We test whether feedback mechanism can directly improve Kalasanty network by adding skip connections from its decoder to encoder.

To further analyze feedback connections, we visualized the output of each iteration for RecurPocket (τ=2). In Fig. 1, $F_{\tau=0}$ refers to no feedback connections, we can find that (i) $F_{\tau=0}$ has more noise and the main part of $F_{\tau=0}$ is incomplete compared with ground truth cavity. After adding feedback connections, we can find that (i) $F_{\tau=1}$ removes the previous noise and enriches the main parts of the prediction; (ii) $F_{\tau=2}$ more focus on prediction sites. Recurrent with feedback connections can remove noise and focus on predictions.
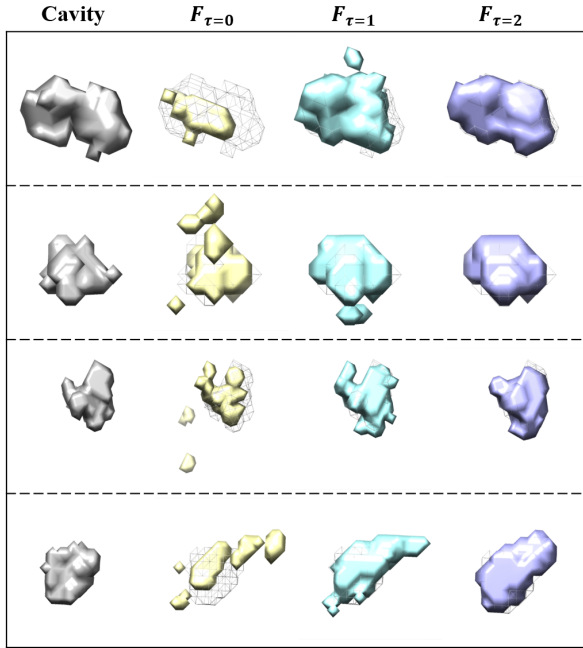

Fig. 1: Each row from left to right is the ground truth cavity (grey), the output of each iteration (τ=0,1,2) of RecurPocket-2 based on Kalasanty settings. The output without feedback connection (τ=0) has a lot of noise, and subsequent feedback connections remove noise and enhance the predicted pocket.

Due to the effect of loss function, feature maps near the output layer will be closer to the ground truth cavity than those in the middle layer, for example, the outputs of the feedback

($F_{\tau=1,2,3}$) in Fig. 1. The information of the feedback comes from the previous decoder, which is usually more close to the result of the prediction site. Such information is resent to the encoder to make it pay more attention to possible sites rather than complex structure of proteins itself or false sites.

B. On DeepPocket settings [2]

Simultaneously, we also evaluate feedback connections and voxel-level masking on DeepPocket [2]. DeepPocket takes candidate local blocks as input, and the centers of these blocks are candidate centers pre-detected by Fpocket [3].
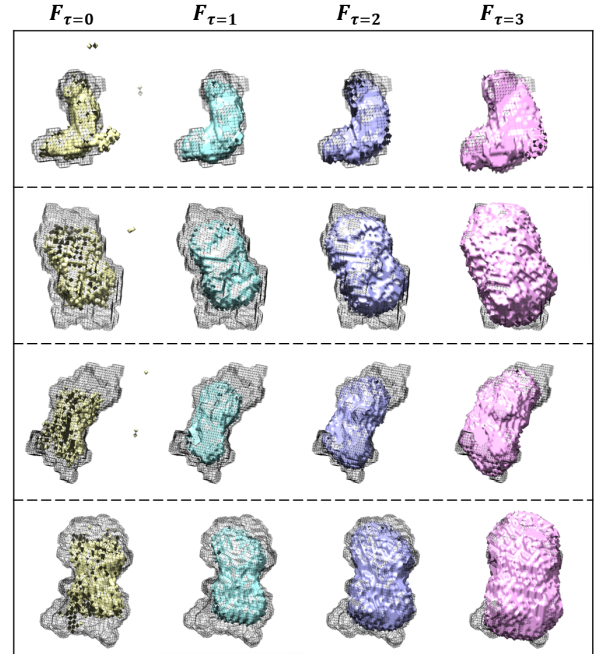

Fig. 2: Each row from left to right is the middle output $F_{\tau=0\sim3}$ of RecurPocket-3. Mesh lines indicate the shape of cavity.

To see what each iteration does, we visualize the intermediate process output of RecurPocket-3 in Fig. 2. It shows the output of each iteration from 0 to 3. We can find that $F_{\tau=0}$ (in yellow) has little noise and incompleteness, and $F_{\tau=1}$ and $F_{\tau=2}$ fix the noise and complete the prediction. But as the τ increases, $F_{\tau=3}$ becomes larger or even beyond the surface of the ground truth cavity, with more false positives. The cavity is more of irregular shapes, but $F_{\tau=3}$ becomes smooth and round, less and less like a cavity with unique characteristics. Increased recurrent times can lead to false enhancements.

References

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[3] Vincent Le Guilloux, Peter Schmidtke, and Pierre Tuffery. Fpocket: an open source platform for ligand pocket detection. *BMC bioinformatics*, 10(1):1–11, 2009.