

## Biological Network Border Detection - Supplementary Information

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### 1 Accessibility perturbation by rewiring the network

In order to assess the sensitivity of the accessibility measure, we performed small perturbations on the studied networks by rewiring the edges and recalculating the accessibility values of the nodes.

The rewiring was performed as follows: for a given edge  $i$ , both its ends were reconnected with probability  $p$  to randomly selected nodes within the first or second neighborhood of the two nodes associated to  $i$ , except the original nodes from both sides of that edge.

Figure S1 depicts the mean error of accessibility, calculated as the average difference between the accessibility before and after the rewiring, considering 30 simulations. For this analysis, the highly connected group of nodes, related to ribosomal proteins, were removed since edge changes within these nodes would drastically impact the network topology.

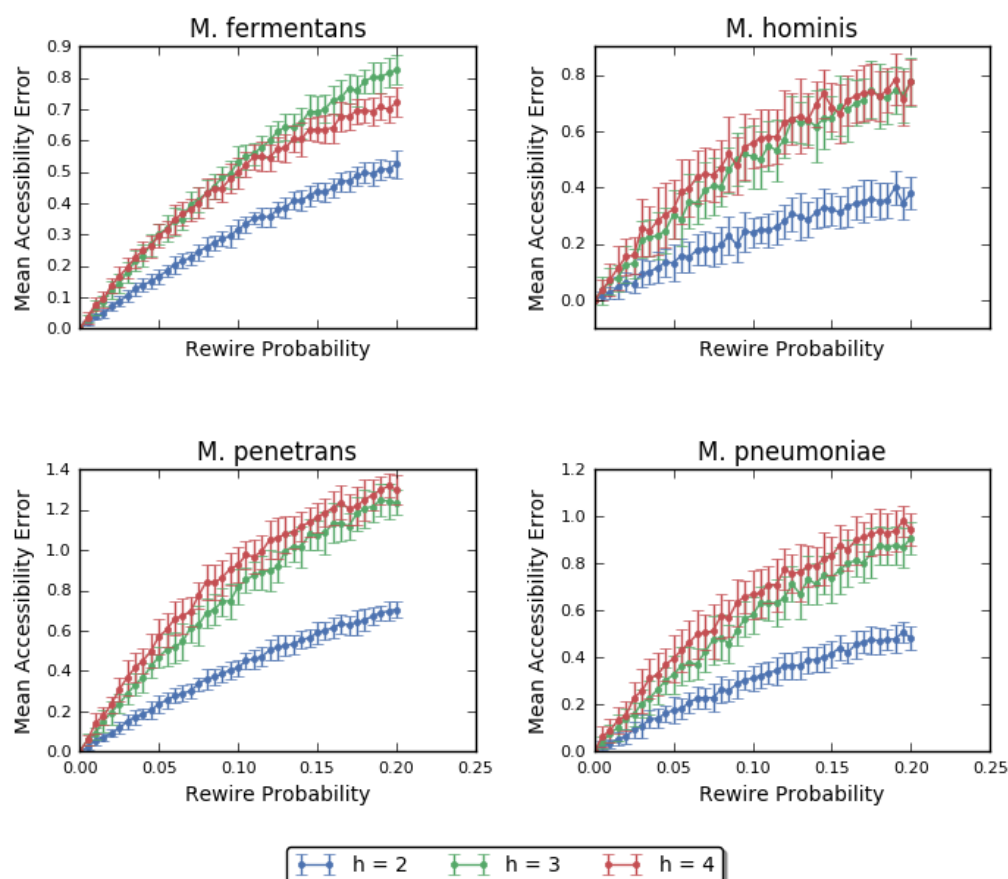


Figure S1: Mean accessibility error for each organism with accessibility hierarchy level  $h$  equal to 2, 3 and 4, for different rewiring probabilities.

Figure S1 shows the mean accessibility of membrane-related GO terms annotated nodes in comparison to the nodes not annotated with membrane-related GO terms. We can observe that for  $p = 0.02$  and  $p = 0.05$ , all networks have a statistically relevant propensity of membrane-related nodes having smaller accessibility values.

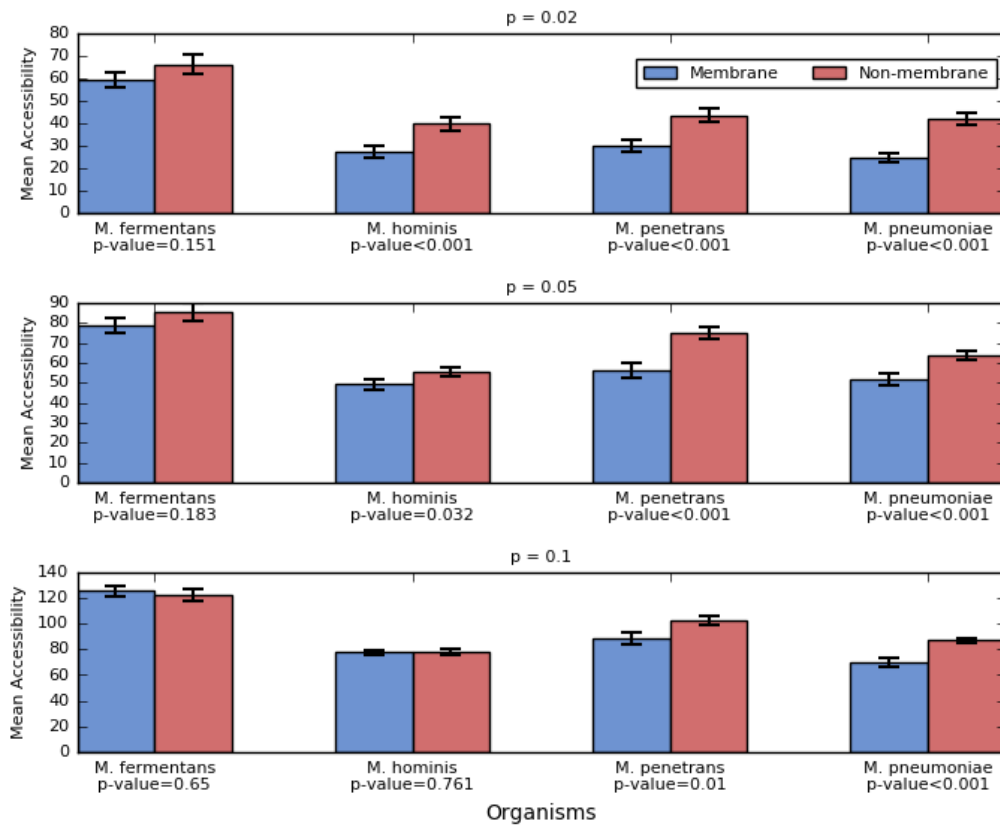


Figure S2: Mean accessibility of membrane-related nodes and non-membrane-related nodes for rewiring probabilities equal to 0.02, 0.05 and 0.1.

## 2 Using degree for topological border assessment

In order to investigate another network measurement related to border detection, we analyzed how the node degree can discriminate between topological border and cell geographical border. More specifically, we compared the mean degree of membrane and non-membrane associated GO terms annotated nodes as shown in Figure 2. The p-values indicate that the results are statistically significant.

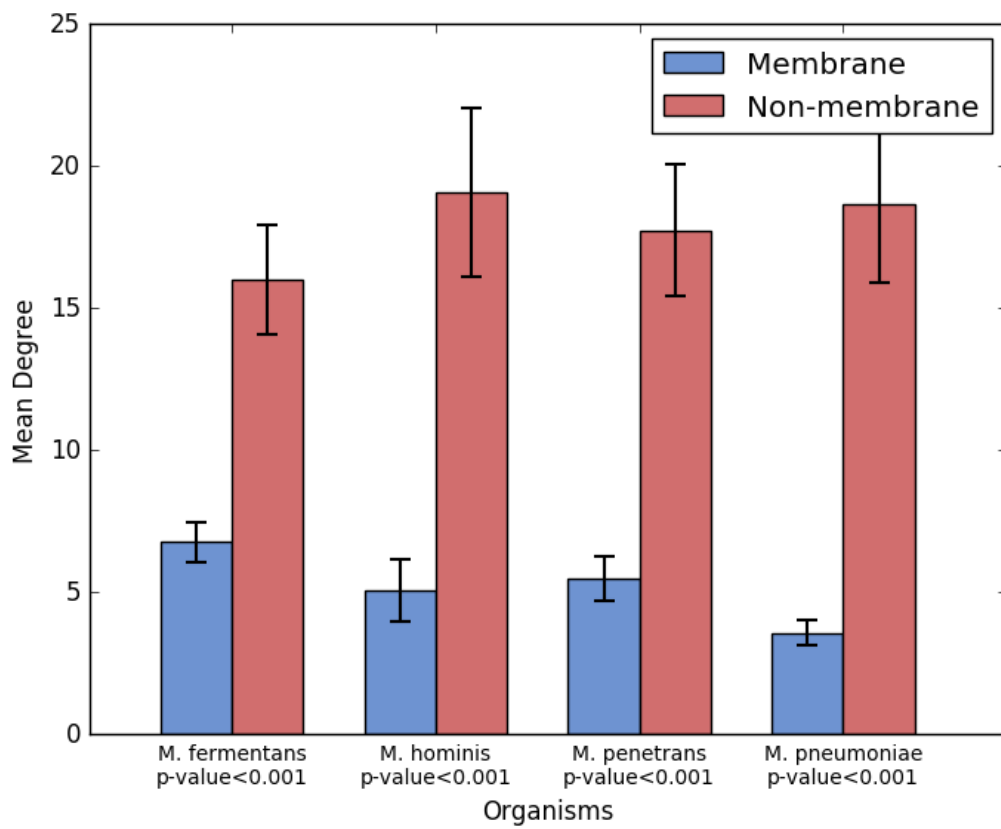


Figure S3: Comparison between the mean degree of membrane-related nodes and the other nodes for each of the four organisms. The error bars indicate the respective coefficients of variation. The p-values obtained for respective t-tests are also shown.