

### S3 Known pathways in extensions

We determined the number of reactions per extension that are associated with a predefined pathway in Metacyc. Fig. 1 shows a histogram of the relative amount of reactions that are part of a pathway for all the extensions of *Chlamydomonas reinhardtii*. About 75% of all found reactions in an extension are part of a known pathway, the rest of the extension was chosen from a set of reactions that are not yet assembled into well-known pathways. Our algorithm is therefore capable of determining novel routes and interconnecting known pathways.

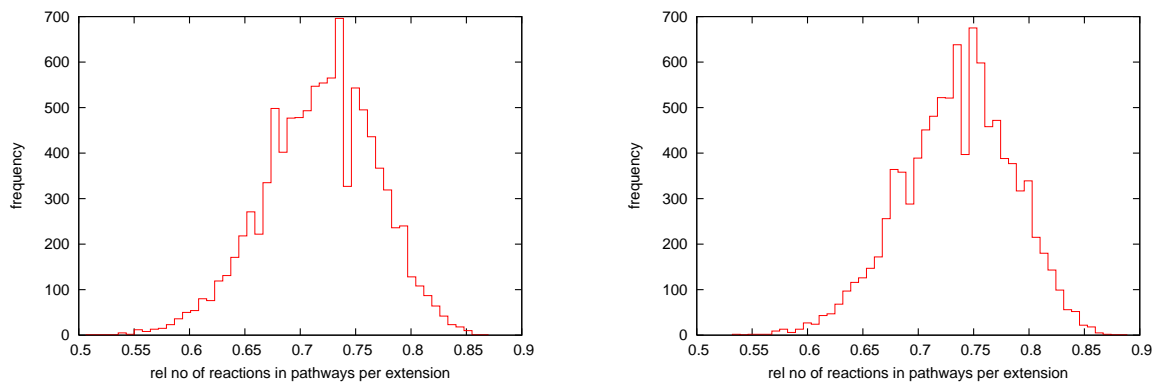


Figure 1: Histogram of the relative number of reactions per extension that are associated with a pathway in MetaCyc. (left) Extensions have been calculated without including sequence information. (right) Extensions were determined including a sequence similarity score.