

**Table 1.** Main characteristics of a panel of gap-filling methods

Name	Input data	Technological platform	Application models
<b>GapFill</b> [1]	Target metabolites	GAMS platform	<i>Escherichia coli</i> strains, <i>Gordonia alkanivorans</i> [2] <i>Salmonella Typhimurium LT2</i> [3] <i>Clostridium beijerinckii NCIMB 8052</i> [4]
<b>FastGapFill</b> [5]	Target metabolites	Matlab & Cplex	<i>E. coli</i> [5] <i>Synechocystis sp.</i> [5]
<b>Meneco</b>	Target metabolites	Python	<i>Ectocarpus siliculosus</i> [6] <i>Candidatus Phaeomarinobacter ectocarpi</i> [7]
<b>Christian et al.</b> [8]	Target metabolites Likelihood of reactions	No available distribution	<i>E. coli</i> [8] <i>Ostreococcus</i> [9] <i>Chlamydomonas reinhardtii</i> [8]
<b>Benedict et al.</b> [10]	Target metabolites Likelihood of reactions	KBase framework	21 bacterial species [10]
<b>Mintz-Oron et al.</b> [11]	Target metabolites Proteomic data	No available distribution	<i>Arabidopsis thaliana</i> [11]
<b>Mirage</b> [12]	Target metabolites Taxonomic weights Co-expression transcriptomic weights	Matlab	<i>Cyanobacteria</i> [12]
<b>Growmatch</b> [13]	Targeted metabolites Growth/no growth data	Matlab	<i>Methanosarcina acetivorans</i> [14] <i>Saccharomyces cerevisiae</i> [15]
<b>OMNI</b> [16]	Flux data	Matlab & GAMS	<i>E. coli</i> [16]

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