

Item	3MCor	M2IA	MaAsLin2	MetagenoNets
Input	Microbiome, Metabolome, Phenotype, Confounders	Microbiome, Metabolome, Metadata	Microbiome, Metabolome, Metadata	Microbiome, Metadata
Metadata type	Continuous, Categorical	Categorical	Continuous, Categorical	Continuous, Categorical
Preprocessing	Missing value imputation, Scaling, Log transformation, Rarefaction, CLR, Pathway deregulation matrix generation	Missing value imputation, Scaling, Log transformation	TSS, CLR, CSS, TMM	TSS, UQ, RLE, CLR CSS, TMM
Intra-correlation analysis	✓	✗	✗	✓
Inter-correlation	✓	✓	✓	✓

analysis				
Global correlation analysis	<p>✓</p> <p>CCA, CIA, PA, O2PLS, Mantel test, sPLS</p>	<p>✓</p> <p>CCA, CIA, PA, O2PLS, sPLS</p>	<p>✗</p>	<p>✗</p>
Hierarchical correlation	<p>✓</p> <p>PCA, PCoA, WGCNA, Variable Ranking within modules</p>	<p>✓</p> <p>WGCNA</p>	<p>✗</p>	<p>✗</p>
(non) Linear identification	<p>✓</p> <p>MIC</p>	<p>✓</p> <p>MIC</p>	<p>✗</p>	<p>✗</p>
Confounders elimination	<p>✓</p>	<p>✗</p>	<p>✓</p>	<p>✗</p>

Correlation method	Pearson, Spearman, Kendall, Partial Pearson, Partial Spearman, Partial Kendall, SparCC, CCLasso, MIC, GRaMM, GLM	Pearson, Spearman, SparCC, CCLasso, MIC	LM, SLM, CPLM, NEGBIN, ZIM	Pearson, Spearman, SparCC, CCLasso, CCREPE, NAMAP
Network analysis	✓ Intra-correlation and Inter-correlation network, Topological indices, Simple Networks Comparison, Hub nodes identification	✓ Inter-correlation network	✗	✓ Intra-correlation and Inter-correlation network, Topological indices, Detailed Networks Comparison
Visualization of Outputs	Global correlation plots, Heat map, Sankey diagram, Circos diagram, Correlation network, Zi-Pi plot, Box plot, Bar plot, Venn	Global correlation plots, Heat map, Correlation network, Circos diagram, Bar plot, Box plot, Scatter diagram,	Heat map, Scatter diagram	Heat map, Sankey diagram, Correlation network, Venn Diagrams, Box Plots

	Diagram, Scatter diagram	Volcano Plot		
Interactive mode	Web and local, Graphical	Web, Graphical	Local, Command line	Web, Graphical
Local deployment	R script	✘	R package	✘
Links	http://3mcor.cn	http://m2ia.met-bioinformatics.cn/	https://huttenhower.sph.harvard.edu/maaslin	https://web.rniapps.net/metagenonets