Higher-order Synthetic Lethality

Where more than 2 genes are SL →

Query   Gene$_X$ Gene$_Y$

→ Function
→ Expression
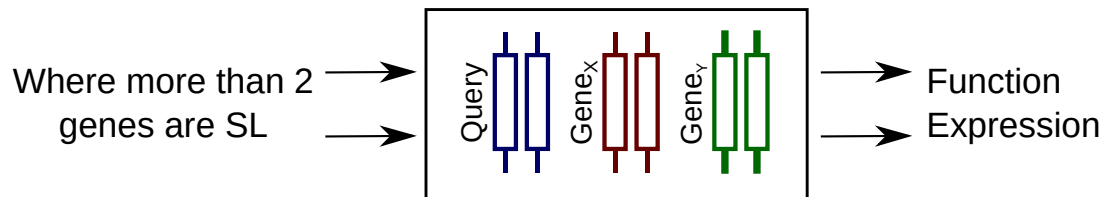
Pairwise SL
One of each pair needed
Stronger Signal

Query

G_X G_Y

Pathway Pairwise
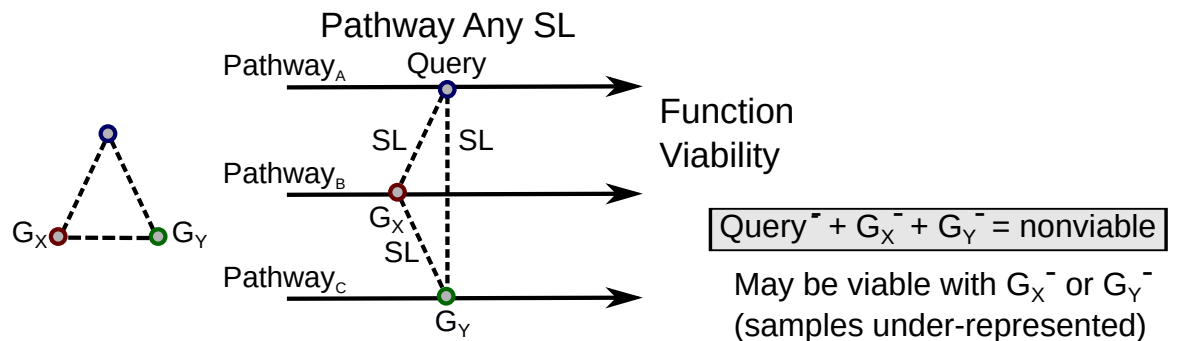
Pathway$_A$ Query

SL   SL

Pathway$_B$ G_X G_Y

Function
Viability

| Query$^-$ + G_X^- = nonviable |
| Query$^-$ + G_Y^- = nonviable |
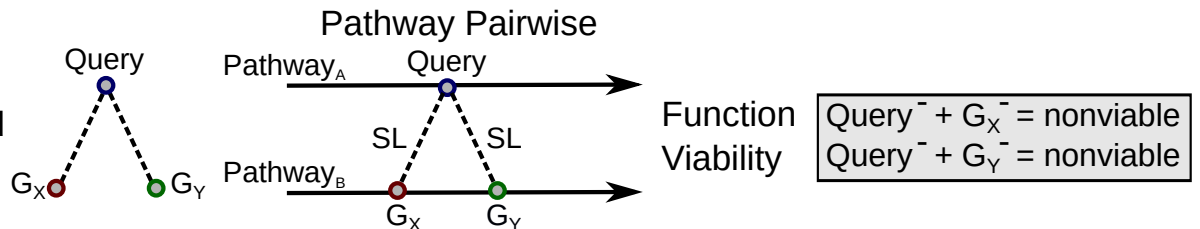
Higher-order SL
Any of triplet needed
Weaker Pairwise Signal

G_X G_Y

Pathway Any SL

Pathway$_A$ Query

SL   SL

Pathway$_B$ G_X

SL

Pathway$_C$ G_Y

Function
Viability

| Query$^-$ + G_X^- + G_Y^- = nonviable |

May be viable with G_X^- or G_Y^-
(samples under-represented)

Samples

	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	. . . .	S_N
Query	+	+	+	+	-	-	-	-	. . . .	.
G_X	+	+	-	-	+	+	-	-	. . . .	.
G_Y	+	-	+	-	+	-	+	-	. . . .	.

Gene Function

Lethal   Not Observed

SL

SL

Under the synthetic lethal model, all SL partners can not be inactivated
but inactive pairs may be detected at lower frequency than expected