Understanding how signaling networks evolve

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Signaling networks: connecting cells with the outside world

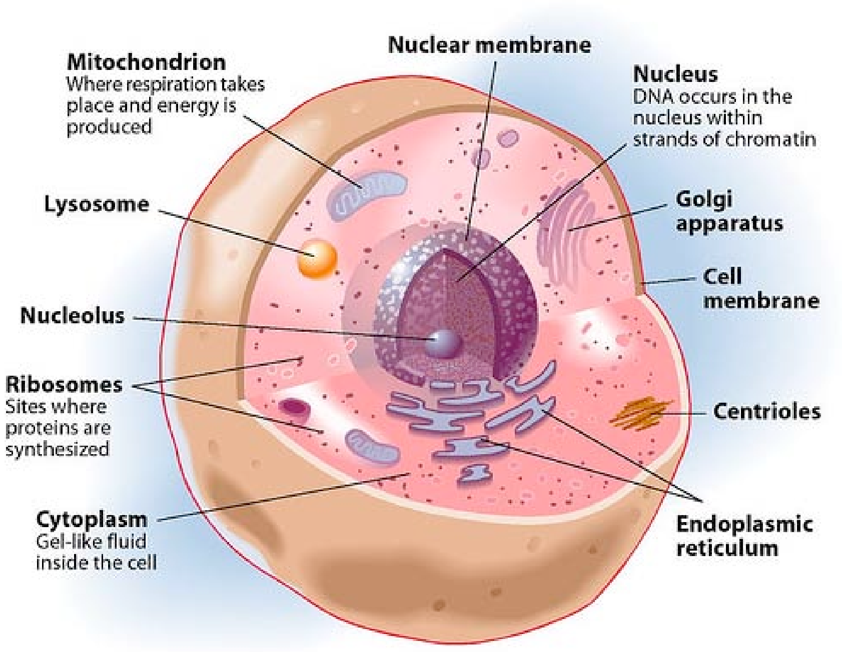

Image: http://nursingcrib.com

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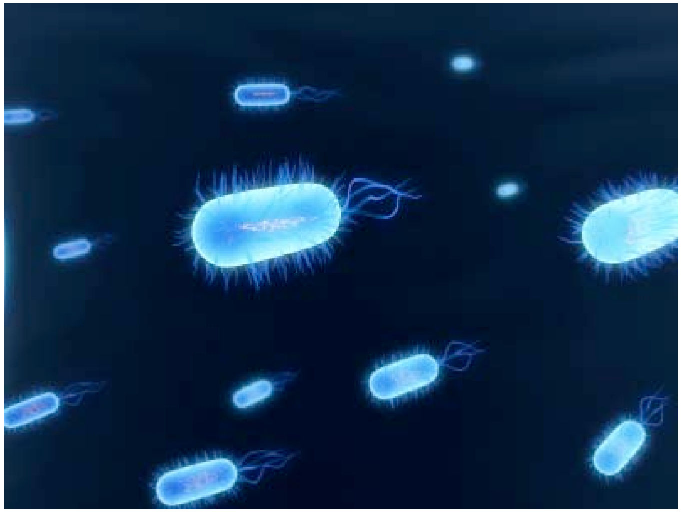

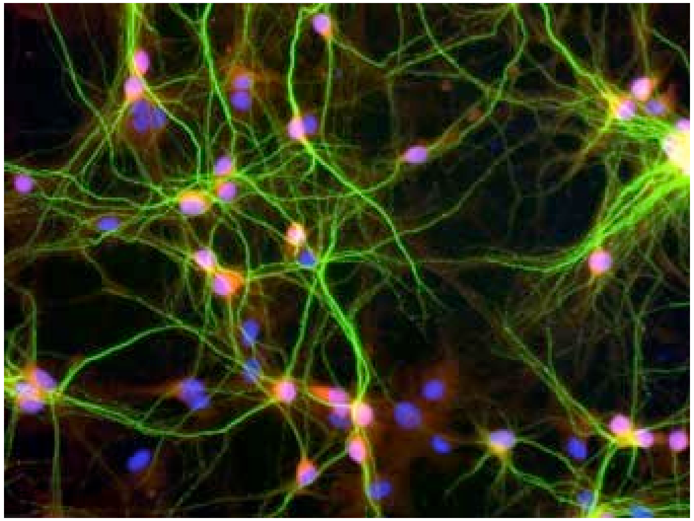

Images: http://www.fi.edu

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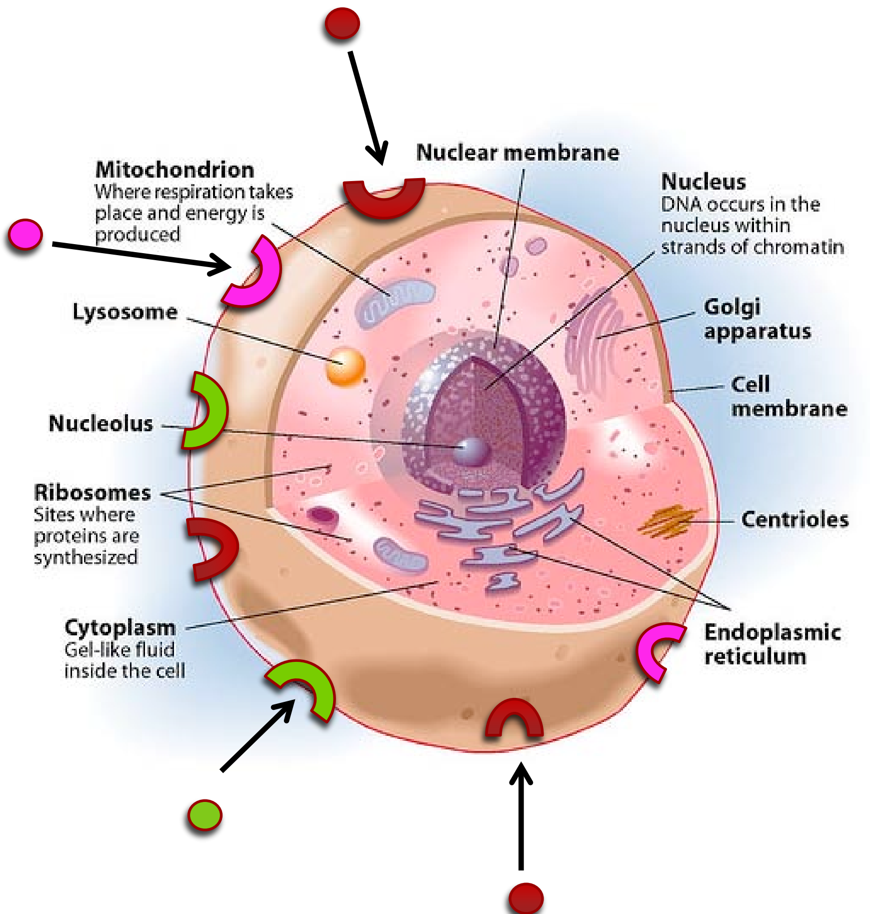

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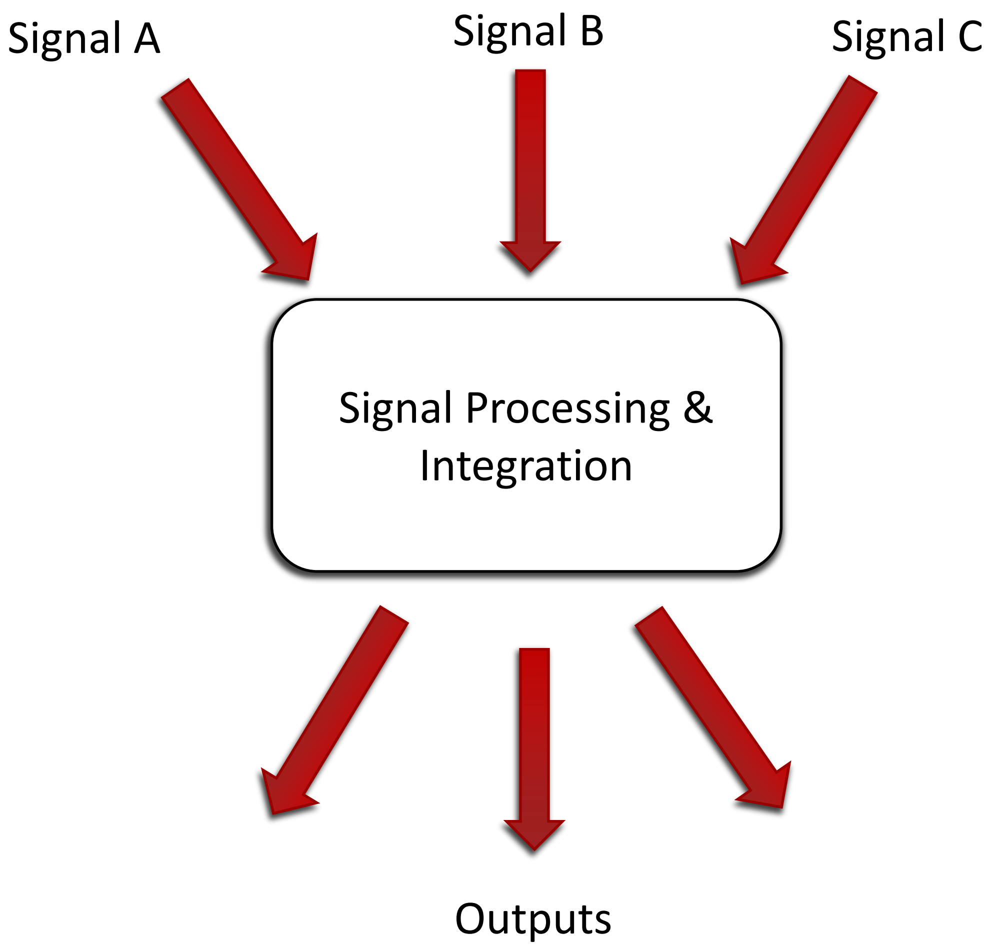
Signaling networks: connecting cells with the outside world



Signaling networks are made of multiple proteins and genes

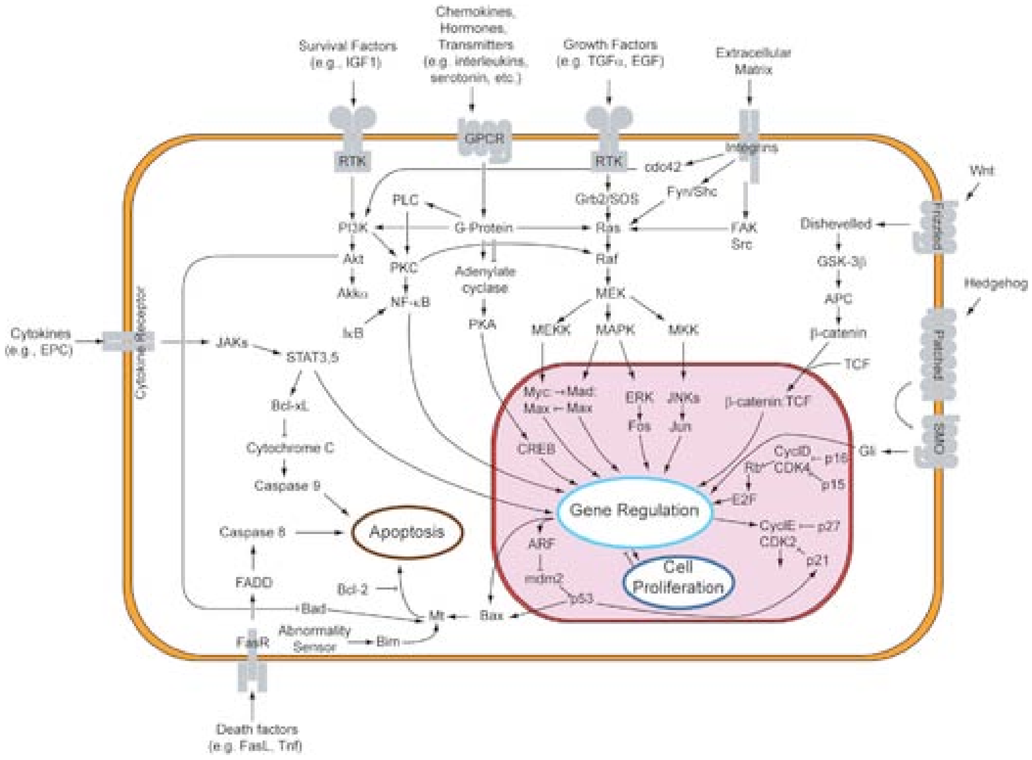
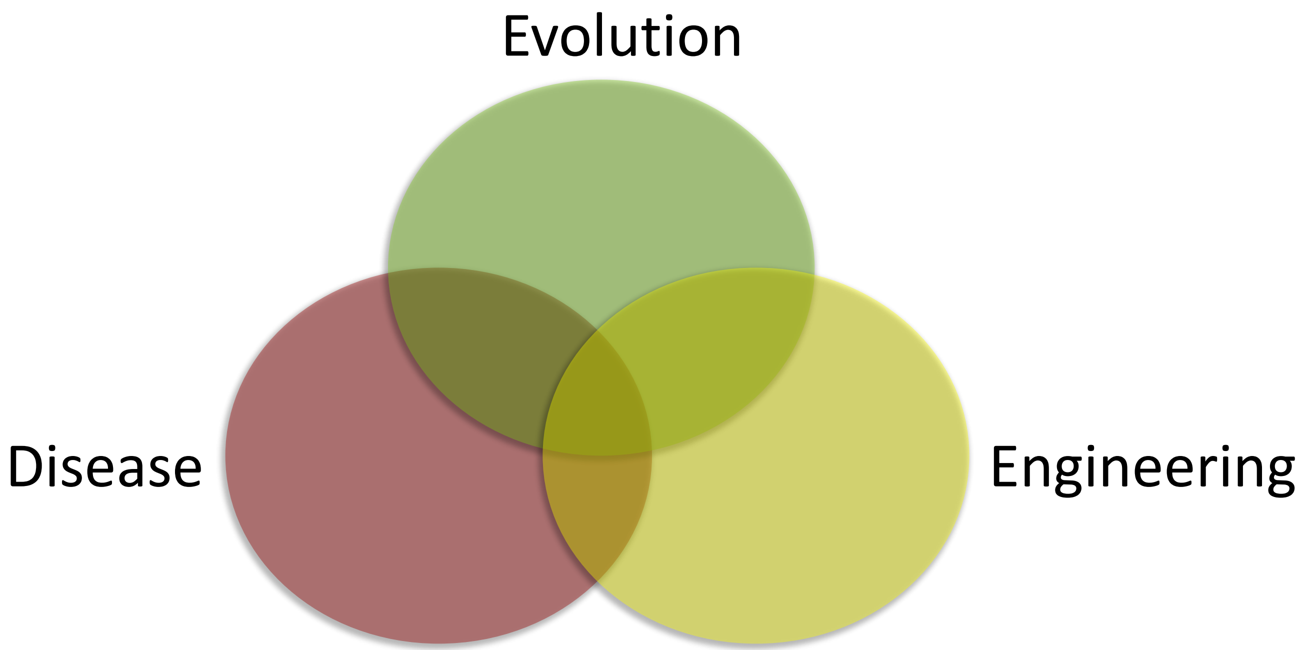
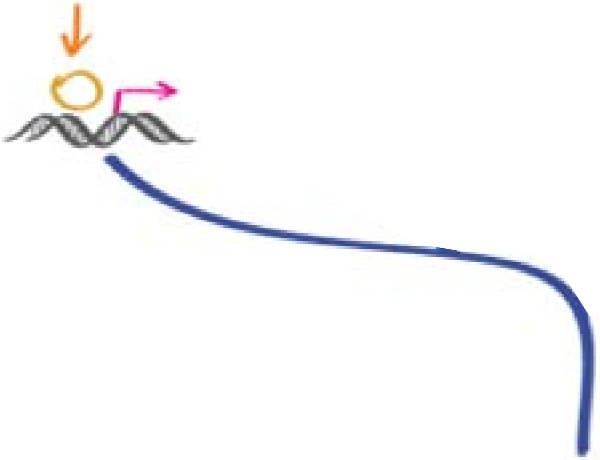


Image: wikipedia

Lab Interests: Signaling Networks



How does this complexity evolve?



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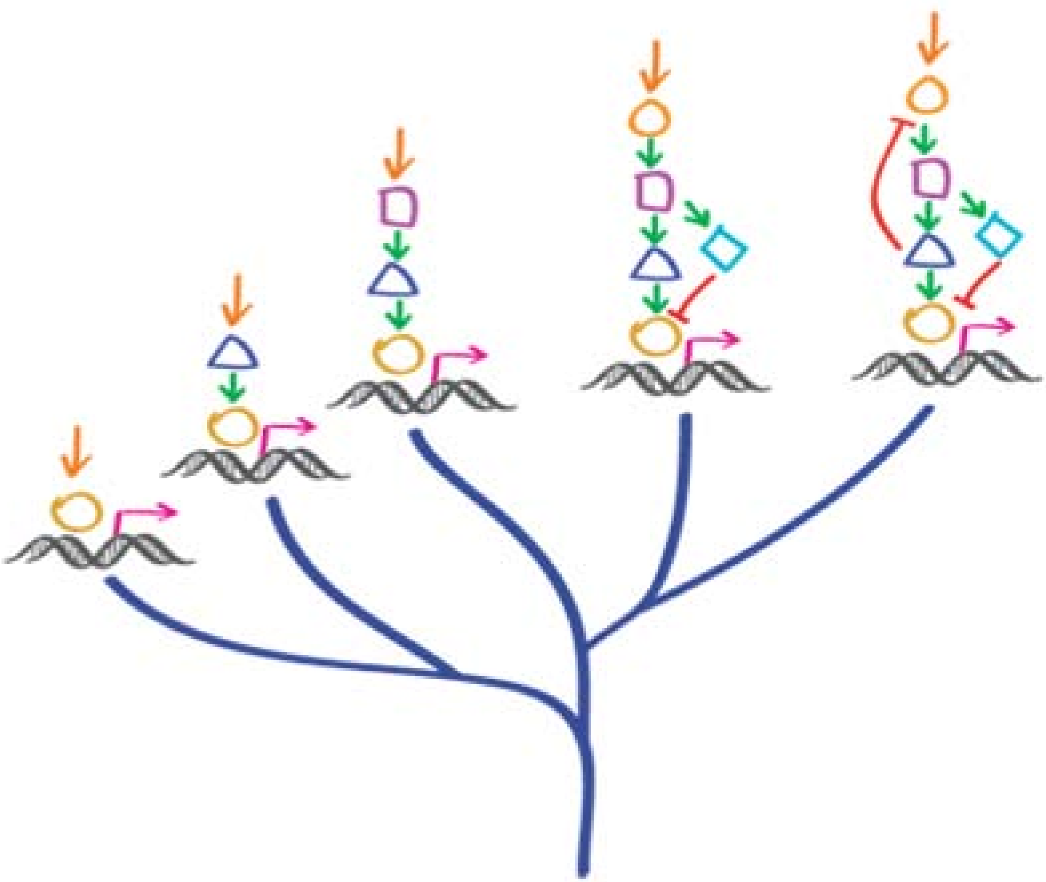

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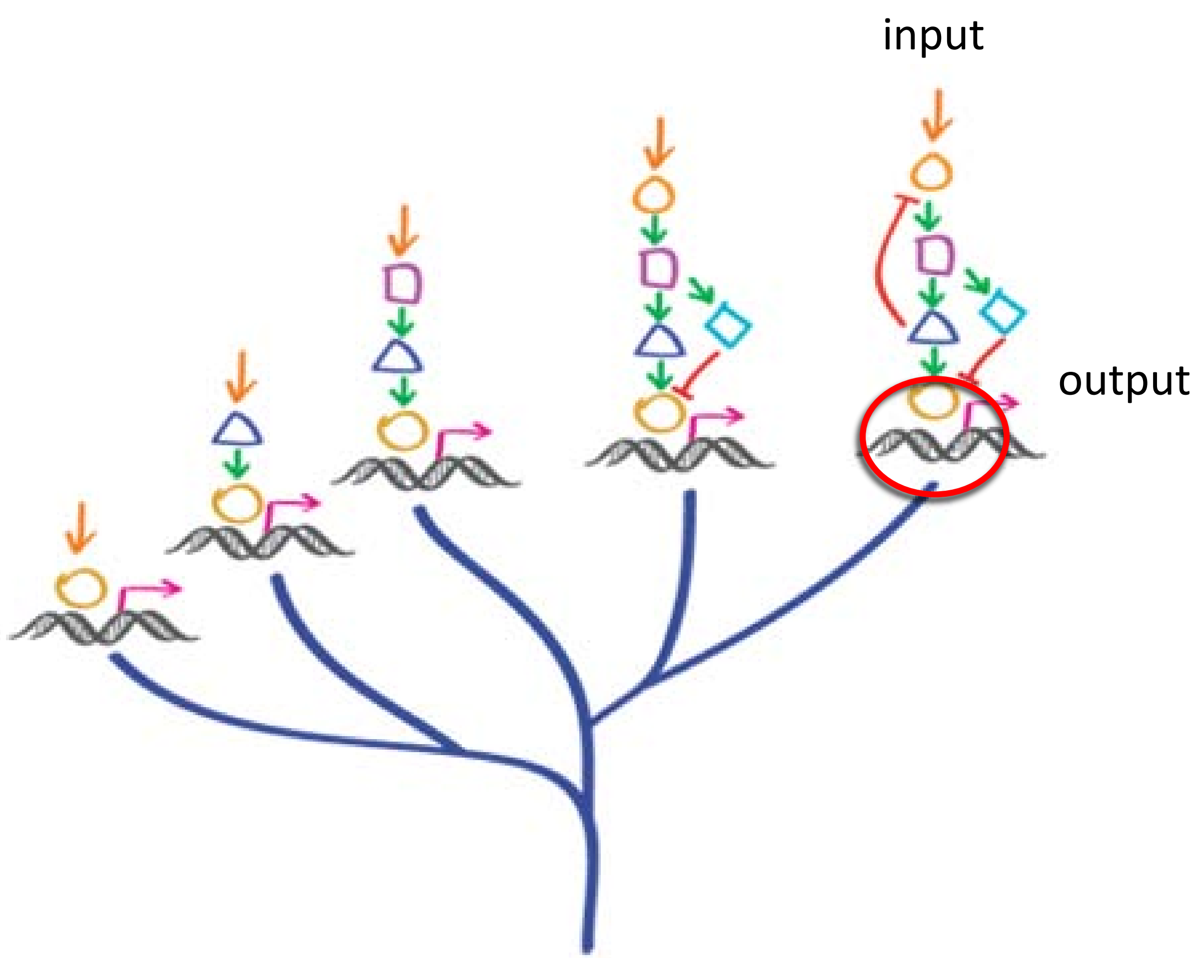
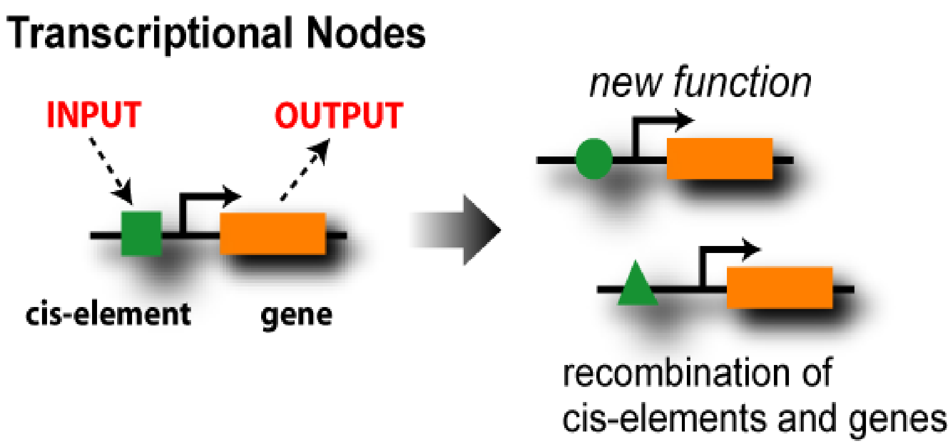


Modularity in Transcriptional Circuits Is Believed to Play an Important Role in Evolution



David Kingsley & colleagues

Sean Carroll & colleagues

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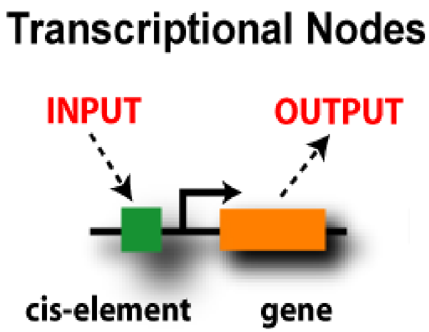
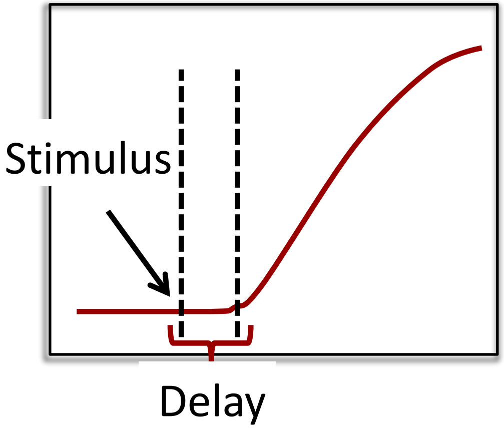
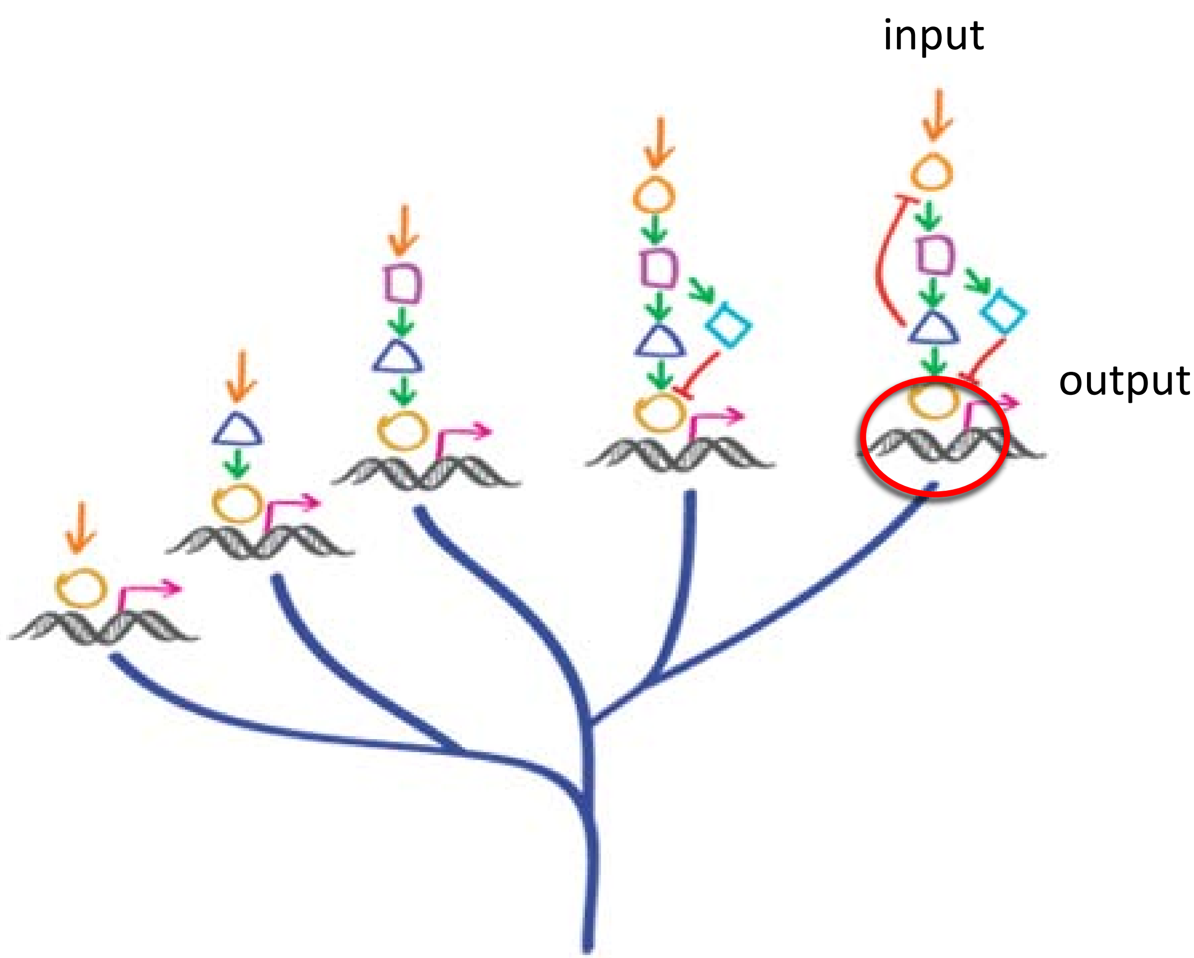




However, evolution mediated by shuffling of genetic elements controlling gene expression is limited to processes that do not need fast responses

How do processes that require faster responses evolve?



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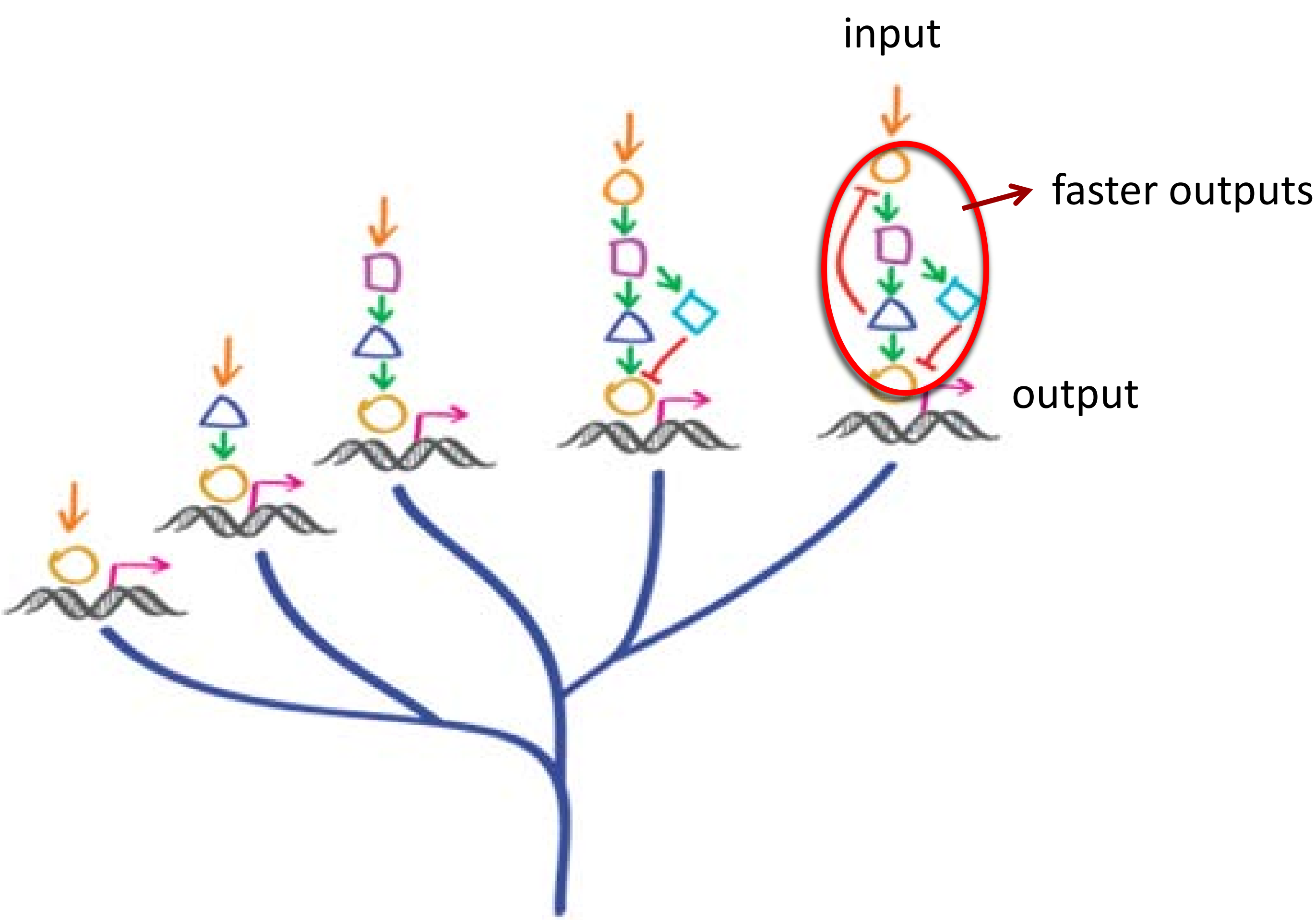
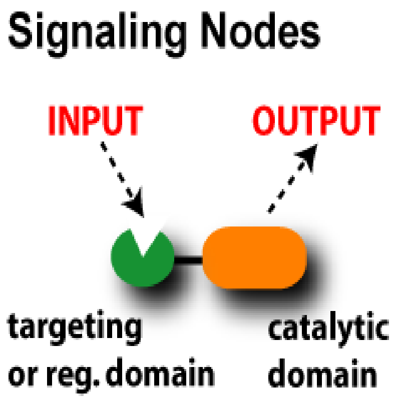
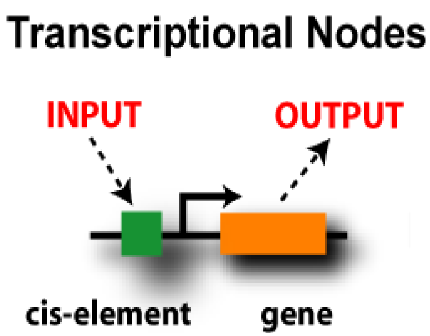
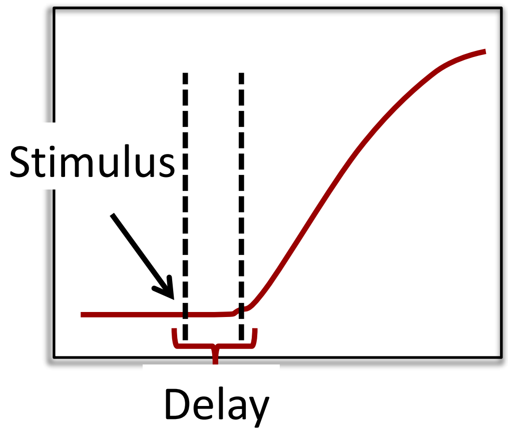


Proteins are organized in distinct domains with modular functions

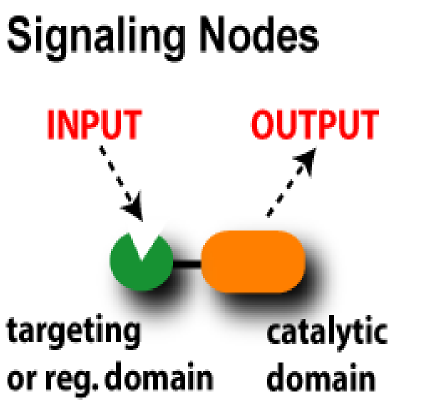


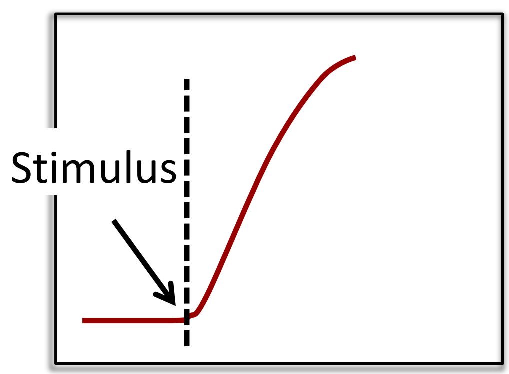
Modularity in protein function regulation could play an important role in the evolution of fast cellular processes





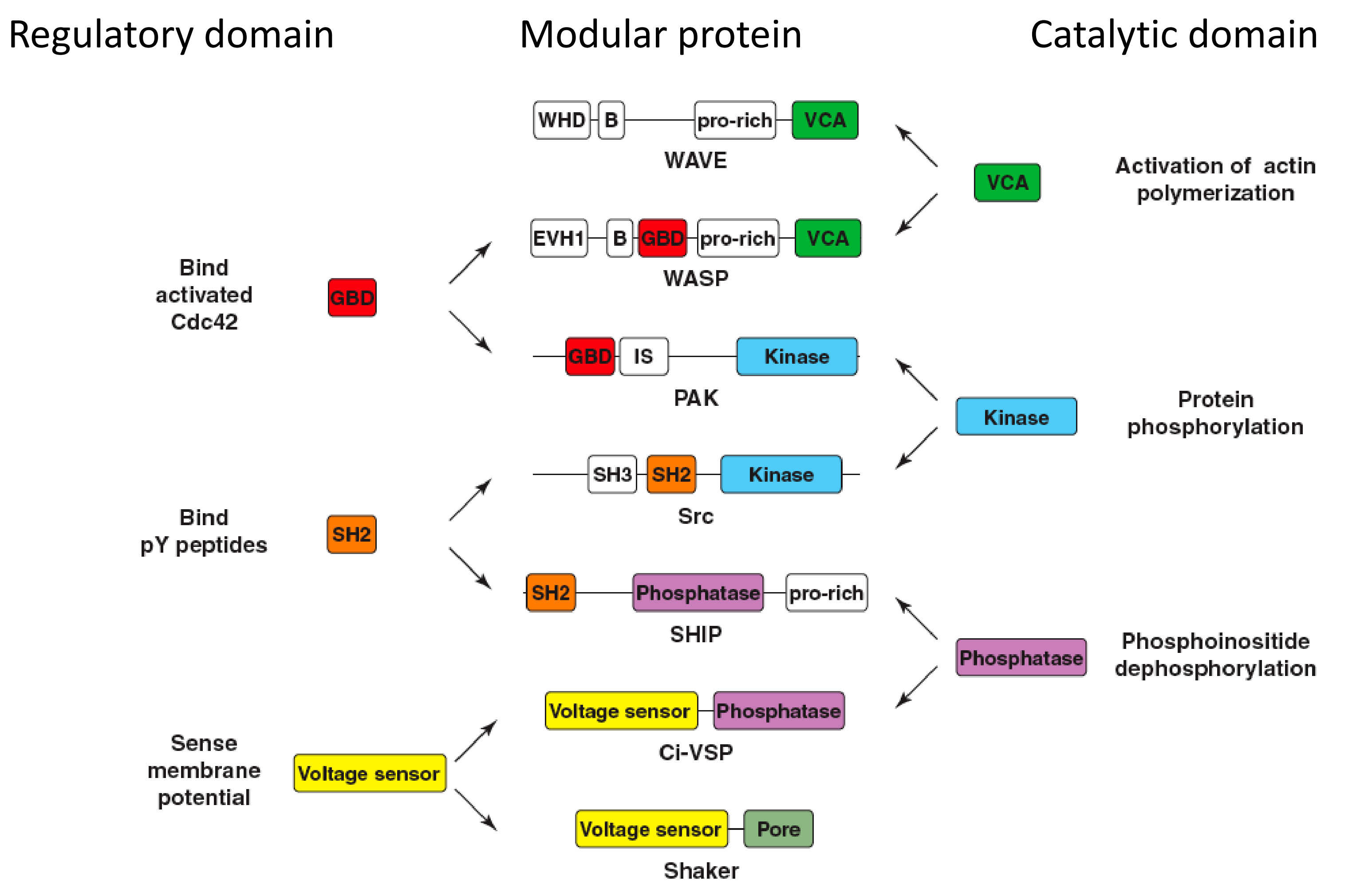
Re-wiring of transcriptional nodes leads to changes in slow responses





Re-wiring of signaling nodes leads to changes in fast responses

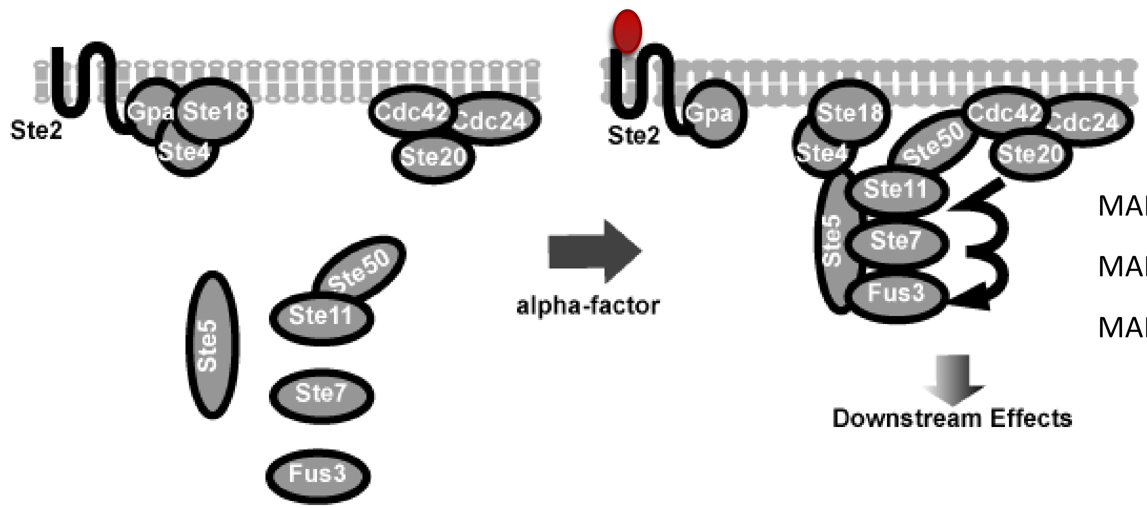
Modular allosteric regulation controls signaling protein functions



One of our research goals:

Exploring the role of protein domain shuffling in the evolution of signaling networks

The Yeast Mating Pathway

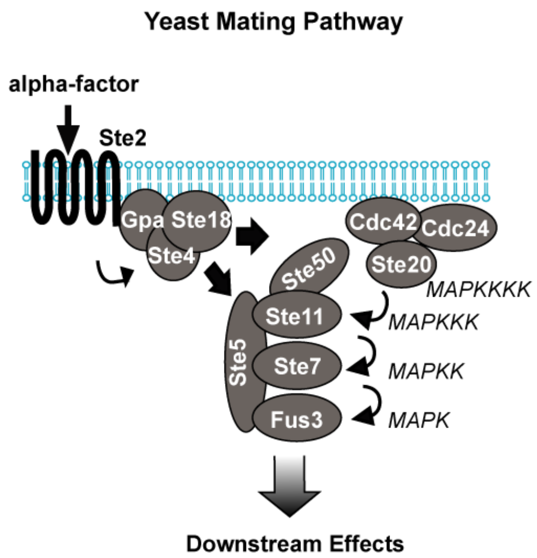


MAPKKK

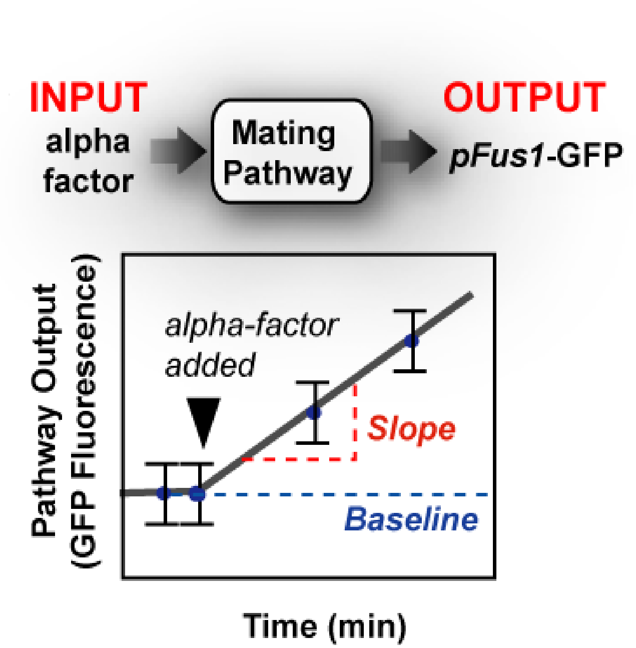
MAPKK

MAPK

Synthetic Biology/Laboratory Evolution Approach



Quantitative Analysis of Large Collections of Strains



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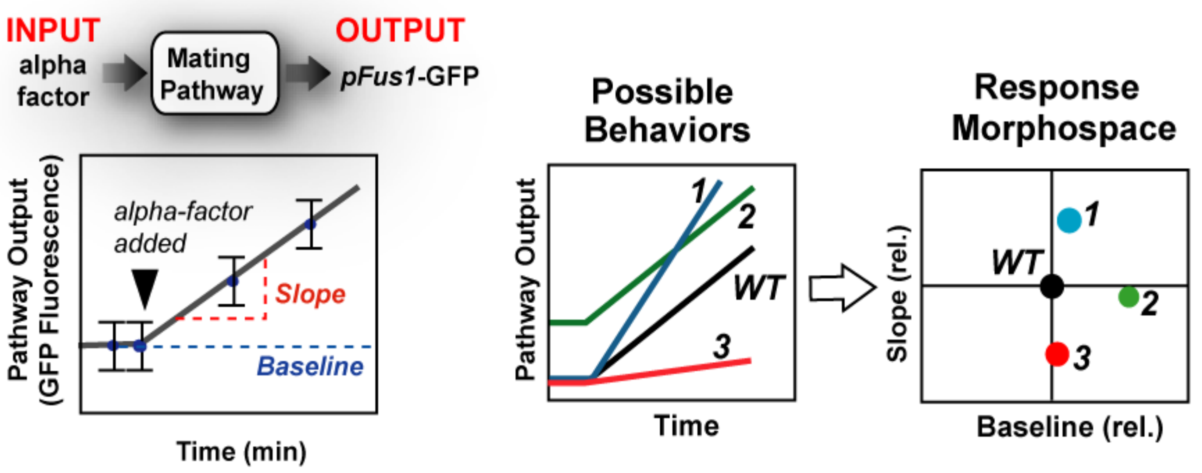
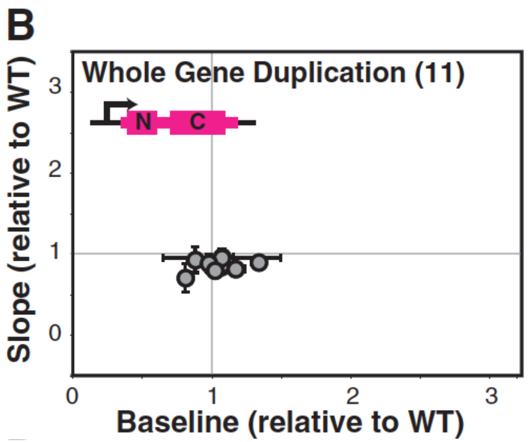
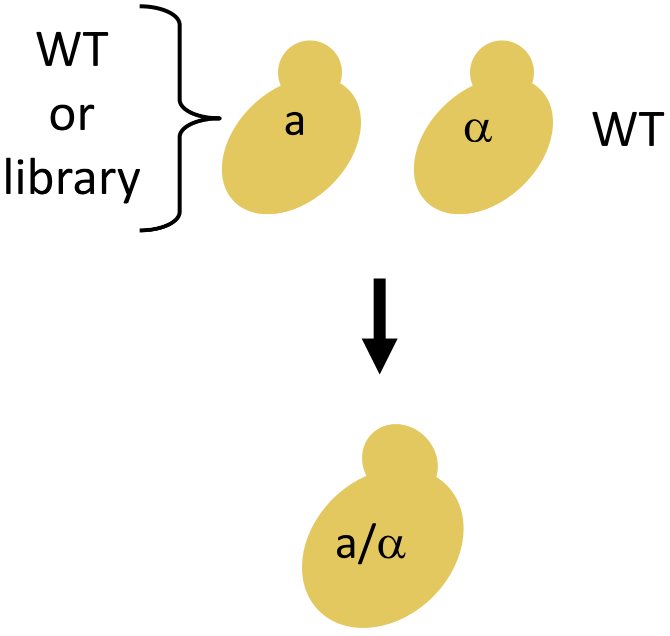


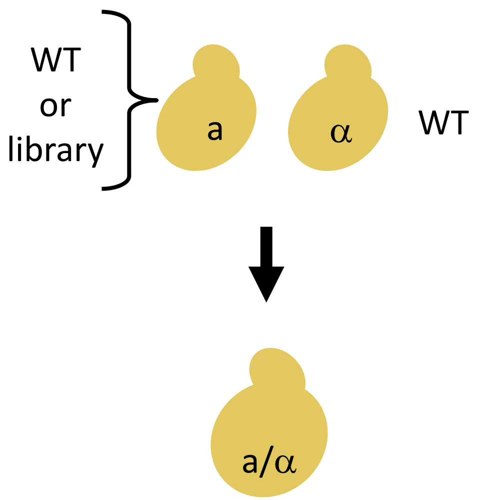
Domain Recombination Leads to Rapid Diversification of Mating Pathway Response Dynamics

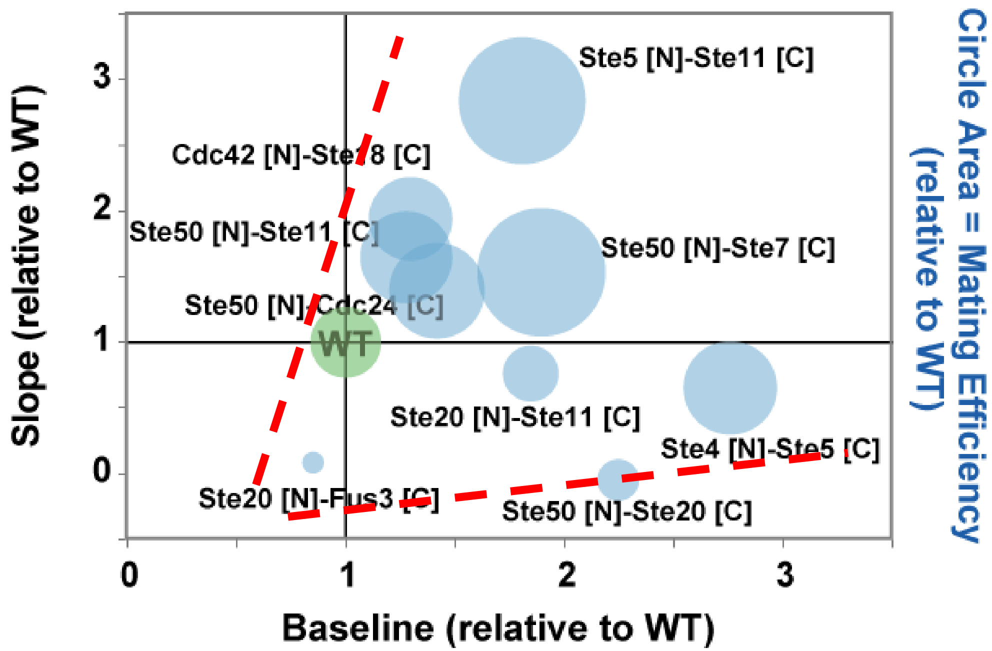


Does Domain Recombination Affect Mating Efficiency as Well?



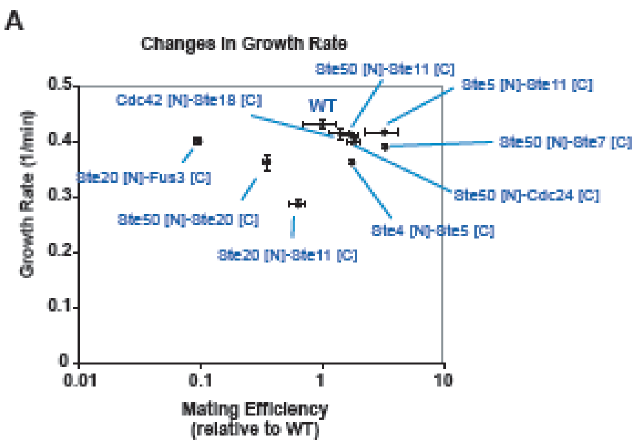
Domain Recombination Leads to Strains that Mate More Efficiently than Wild Type





Why are there variants that mate better than WT (in the lab)?

The fitness cost of pleiotropic effects could be balanced by gains in mating efficiency



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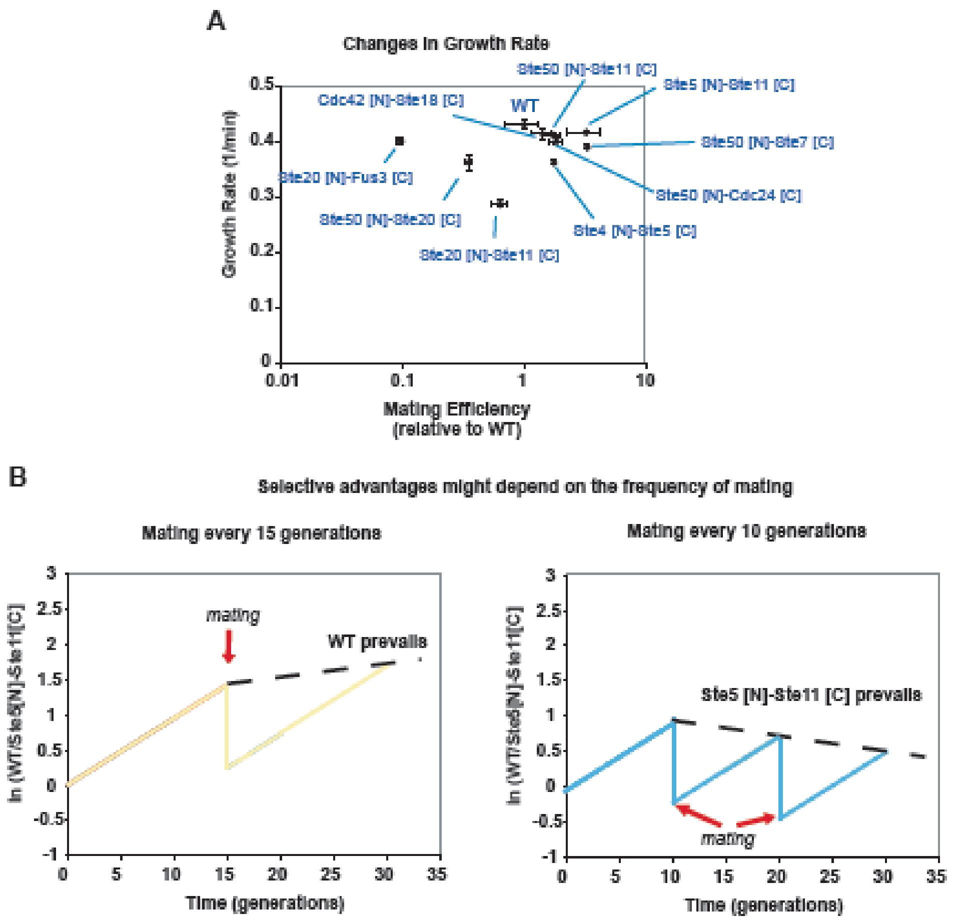
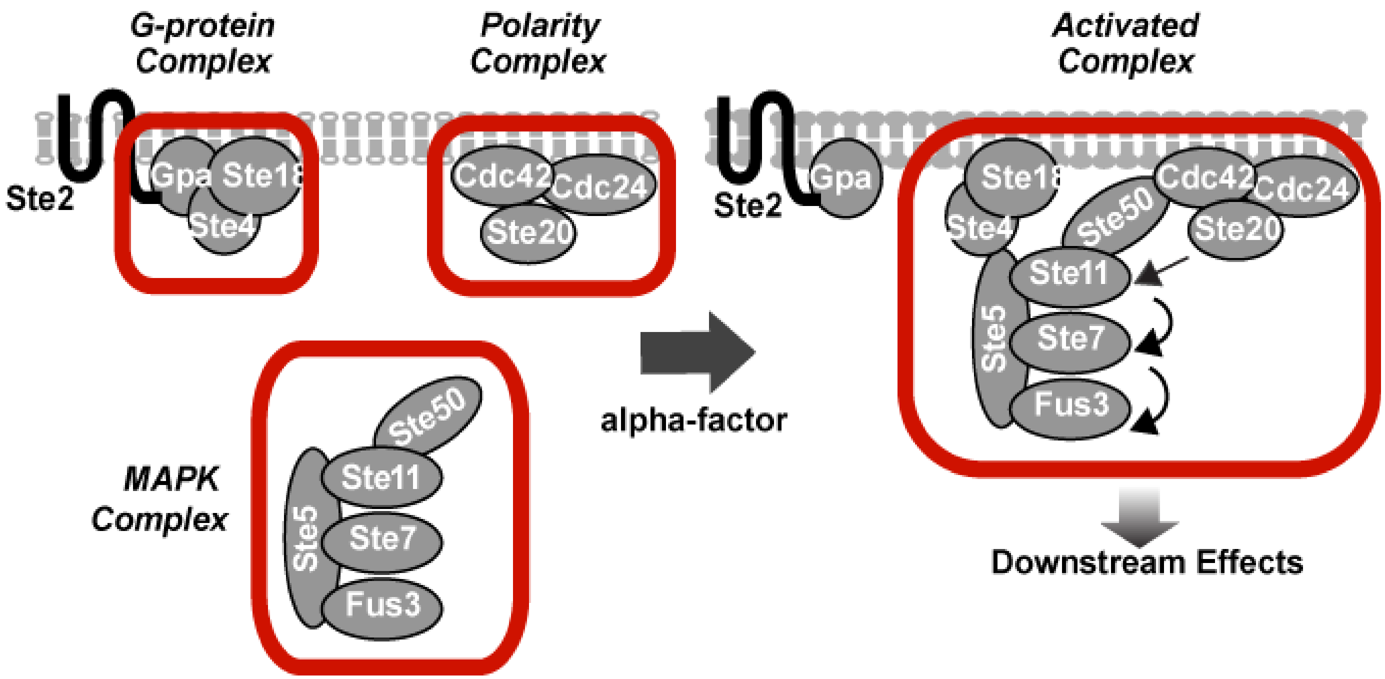
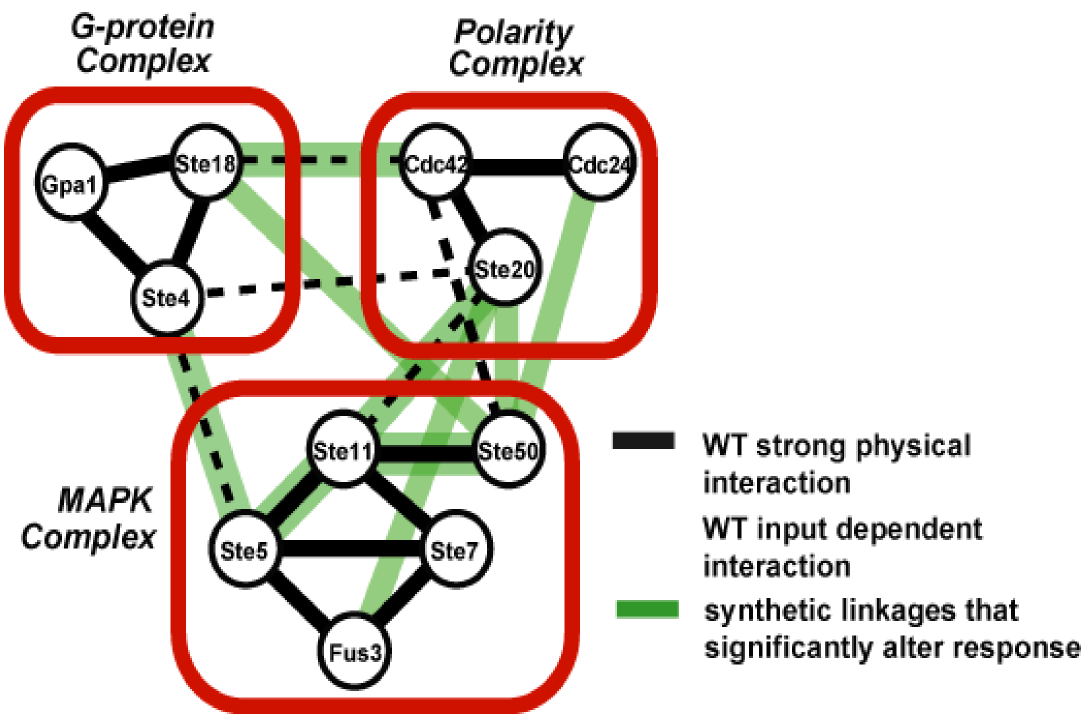


Understanding the Mechanisms that Result in Response Changes



Fluorescence Microscopy Experiments Suggest Possible Mechanisms Leading to Changes in Response Dynamics



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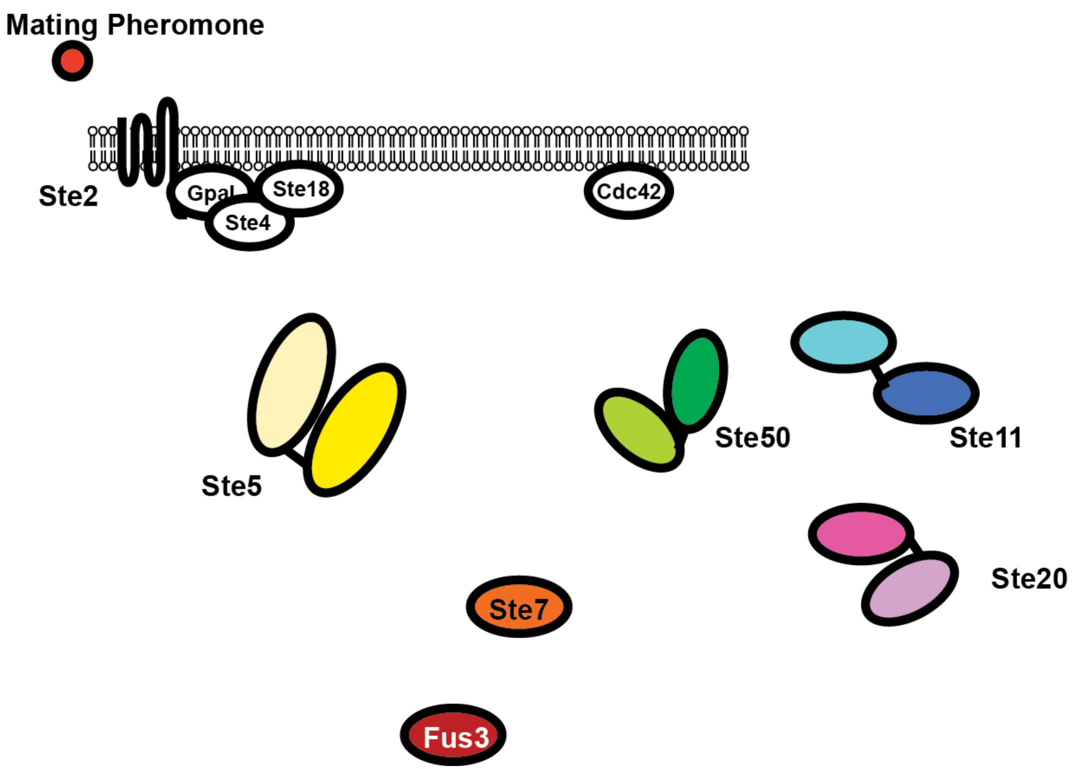

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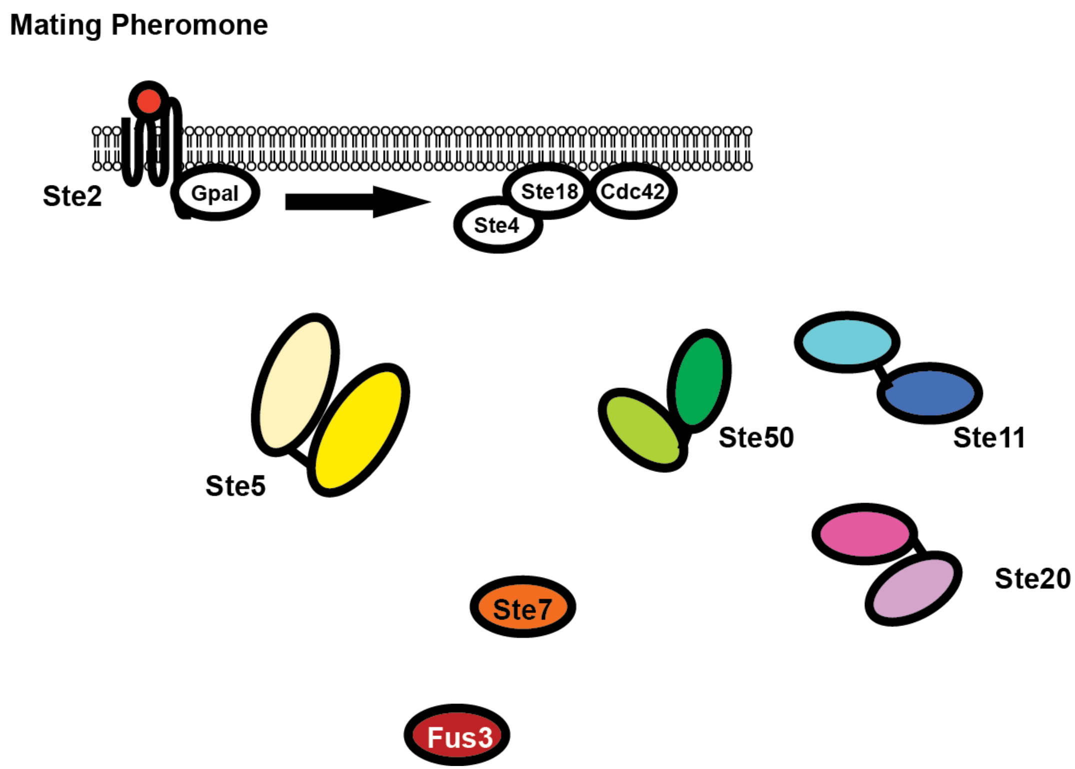

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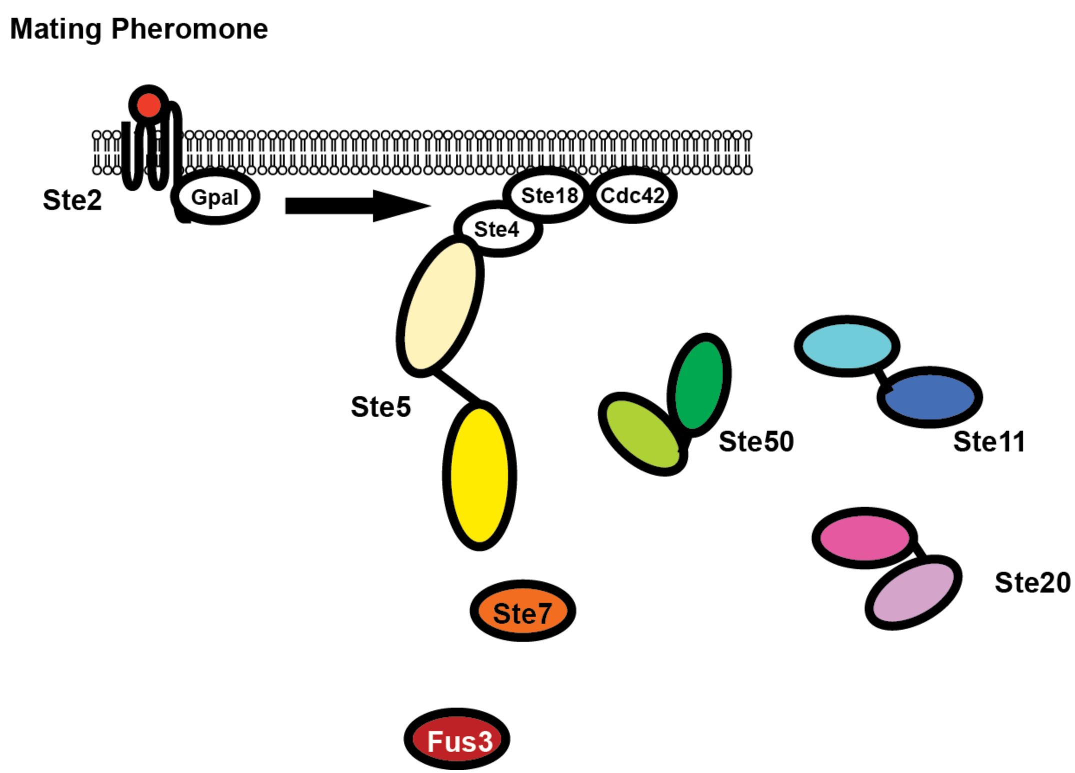

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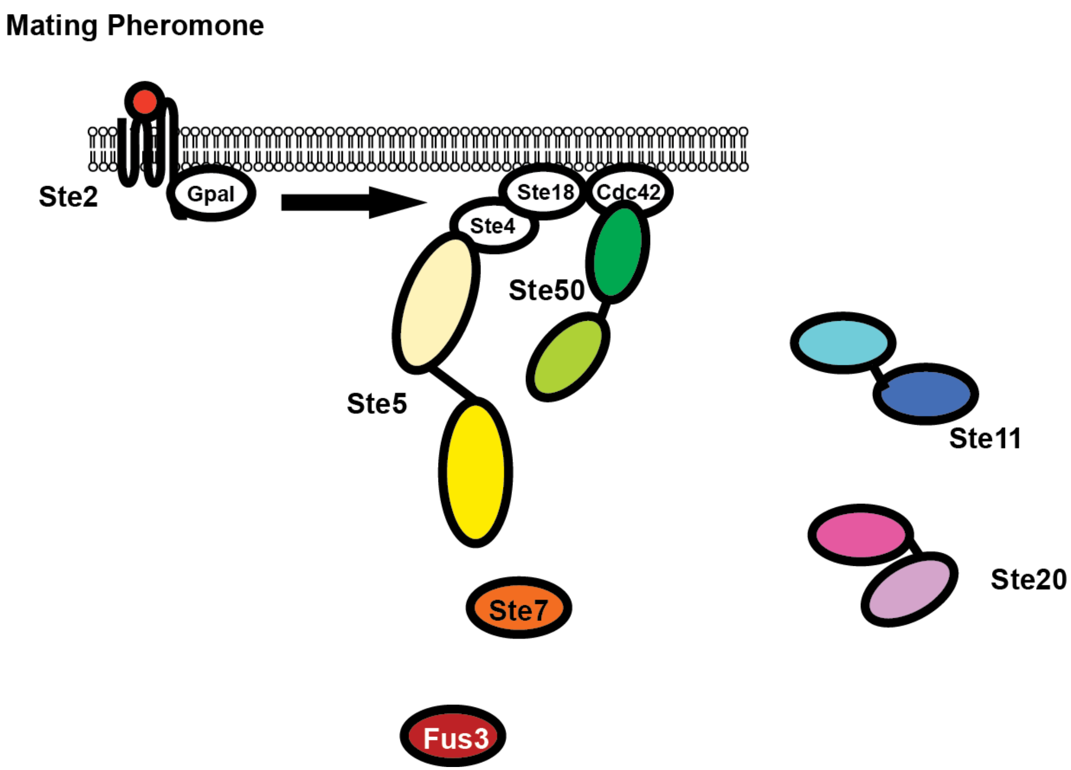

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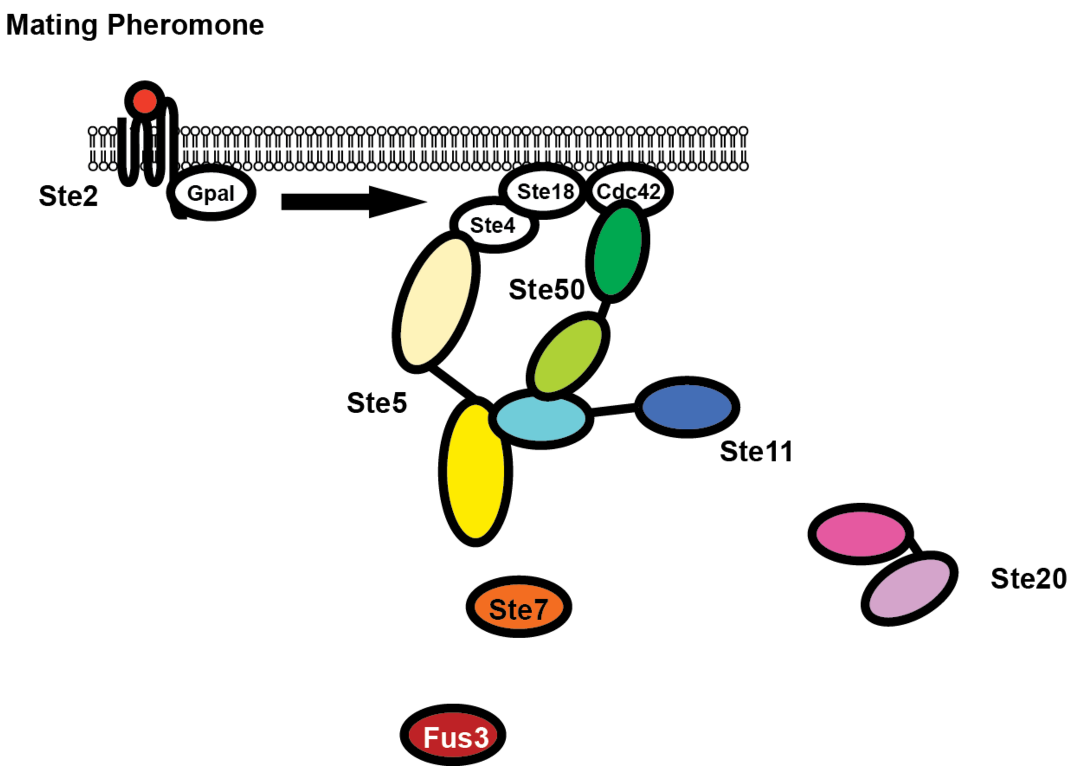

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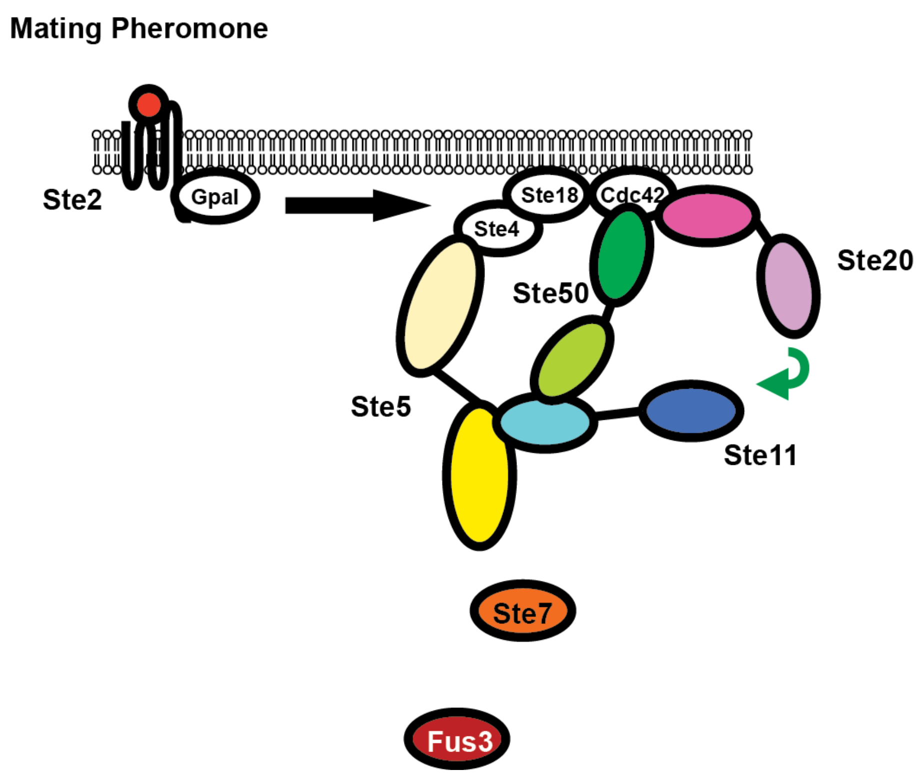

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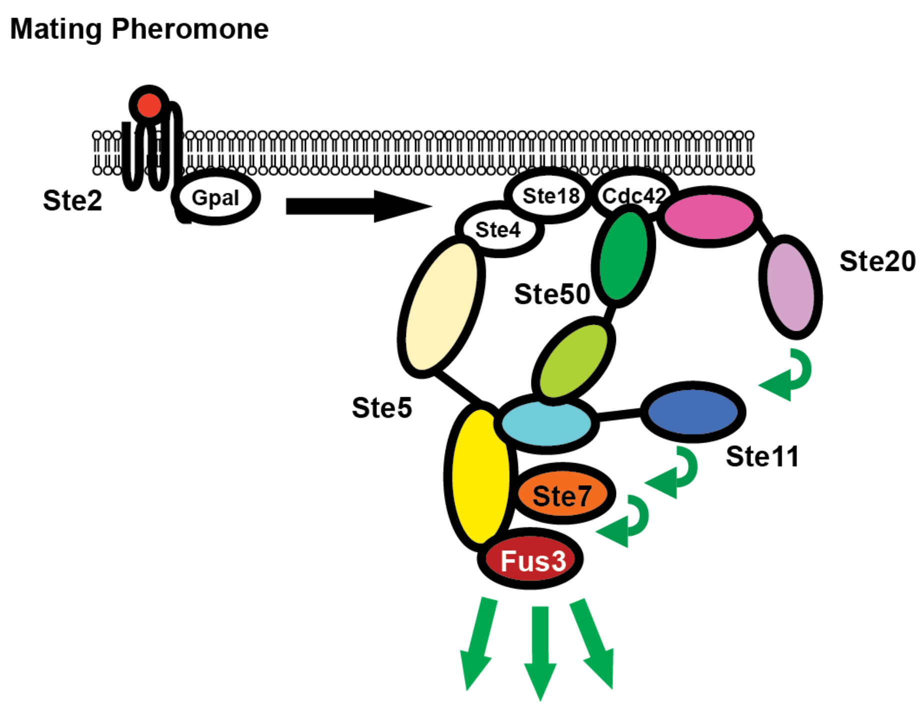

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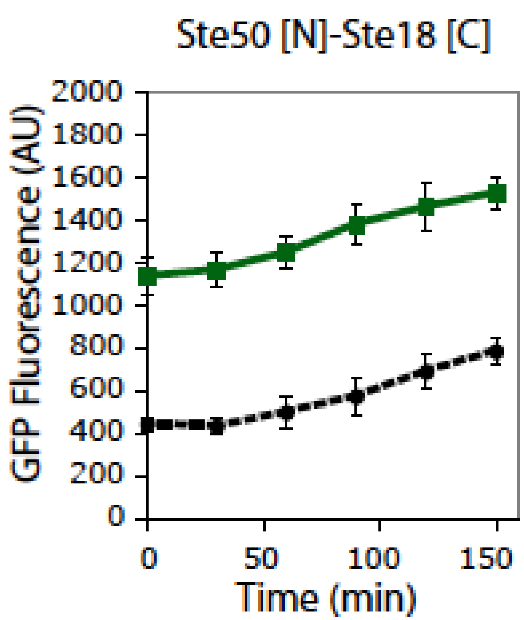

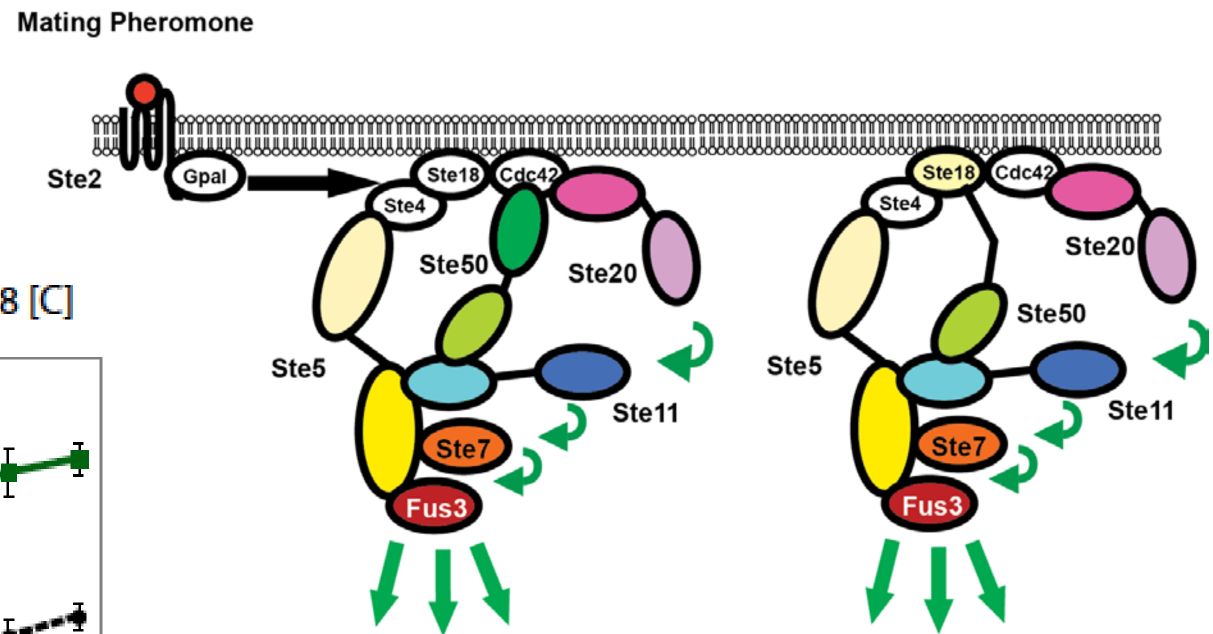

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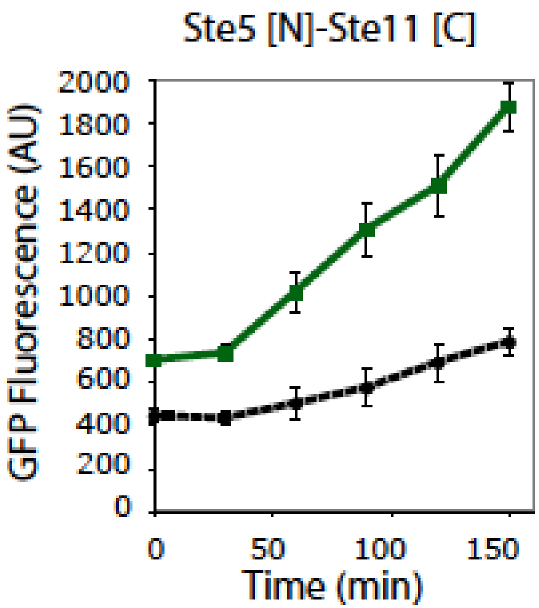

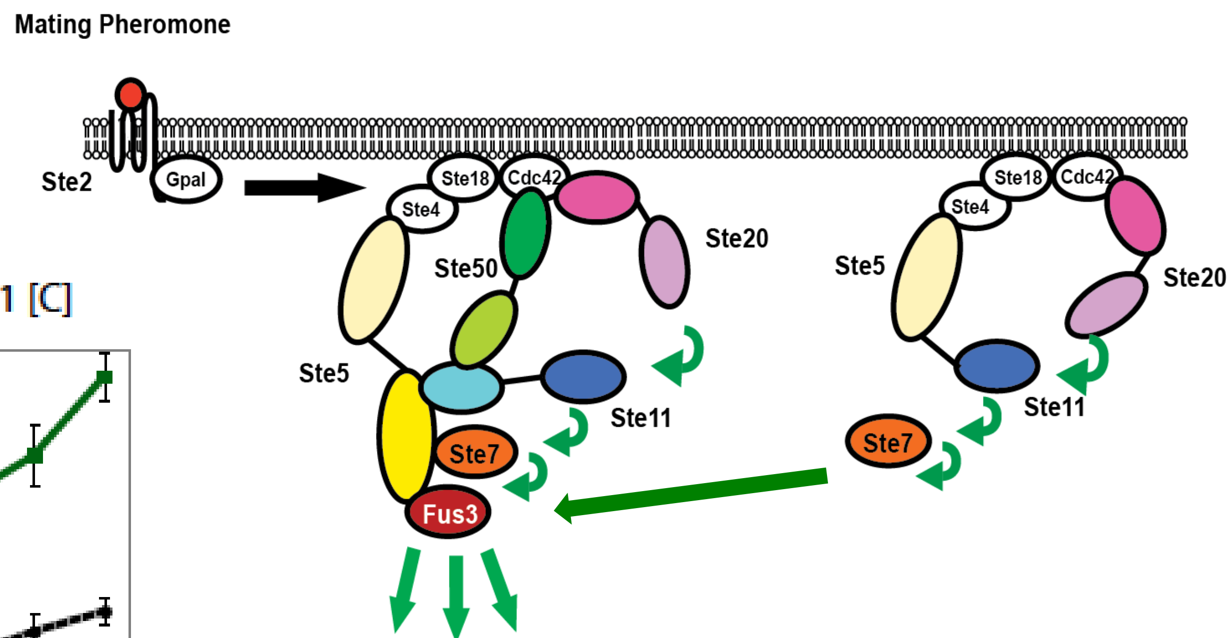

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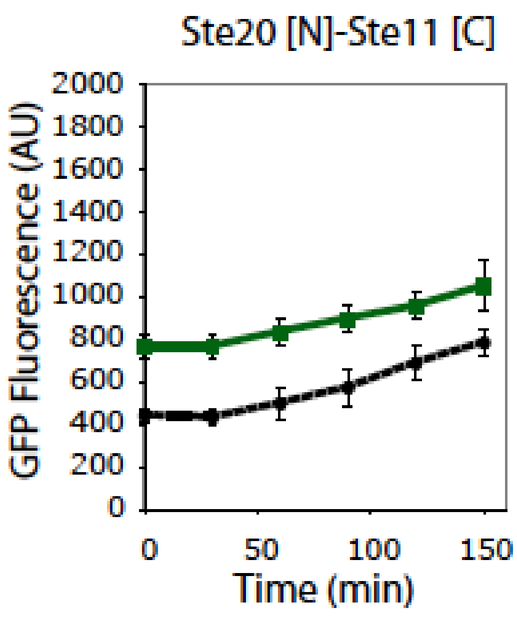
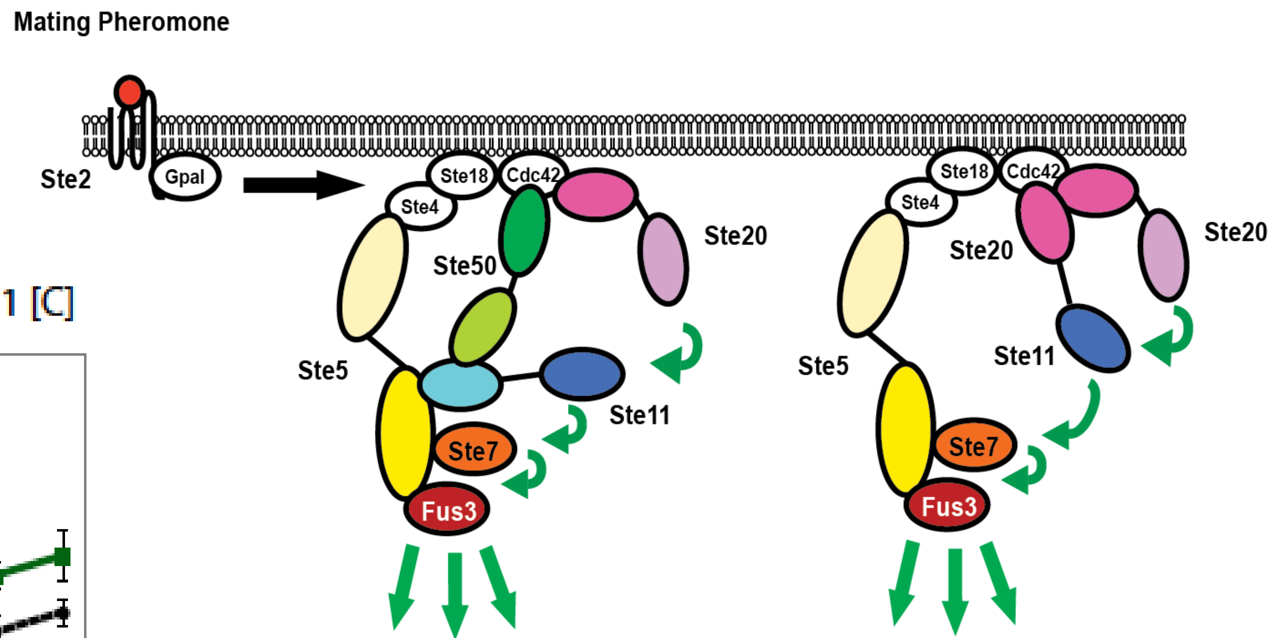
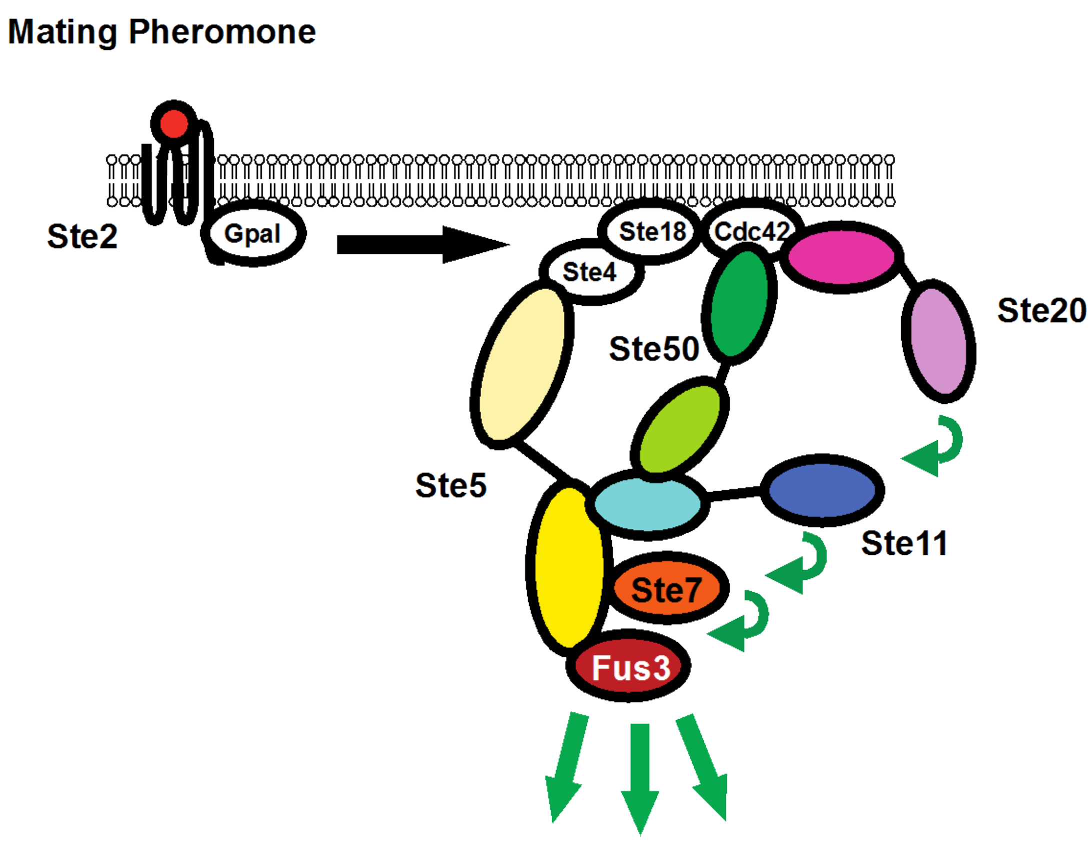




Would domain recombination still lead to adaptive evolutionary change when at least one wild type gene is deleted?



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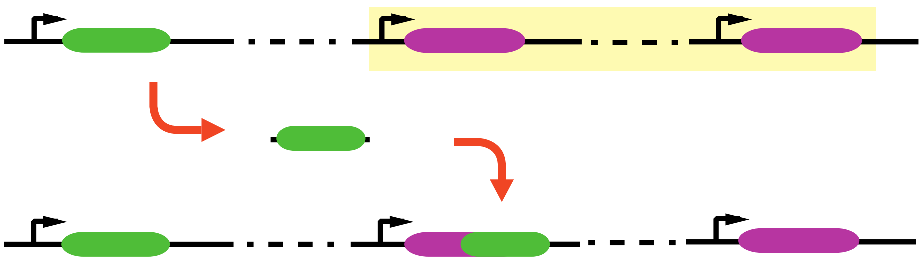
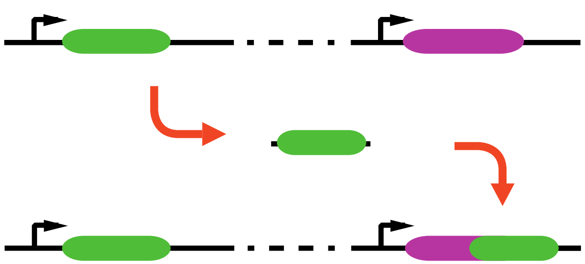
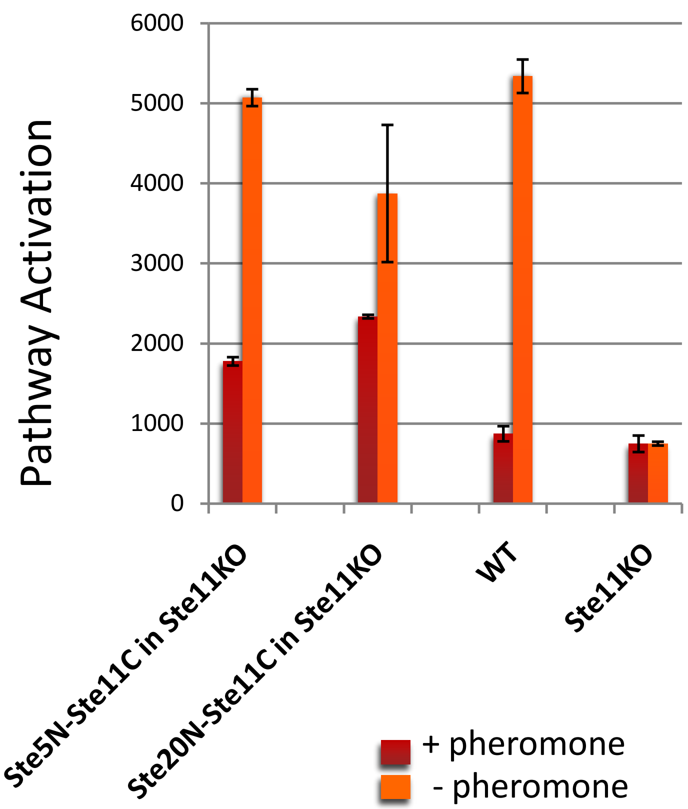
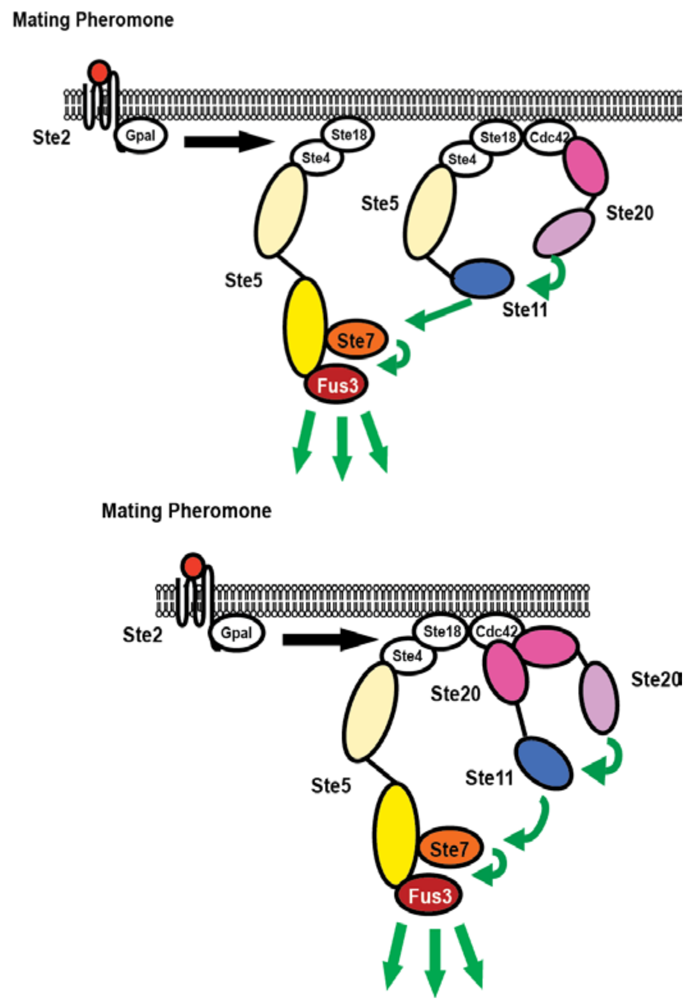


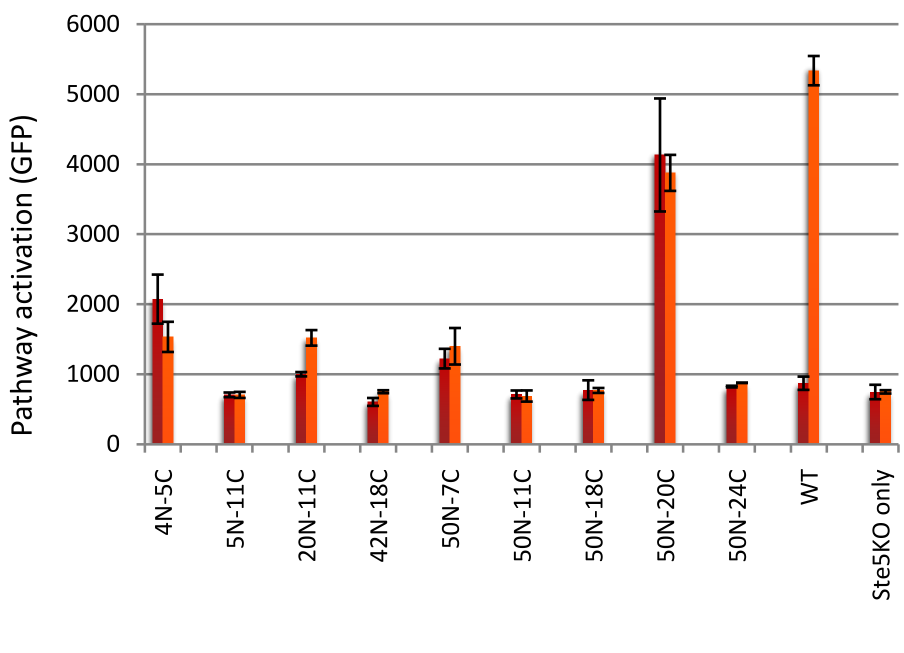


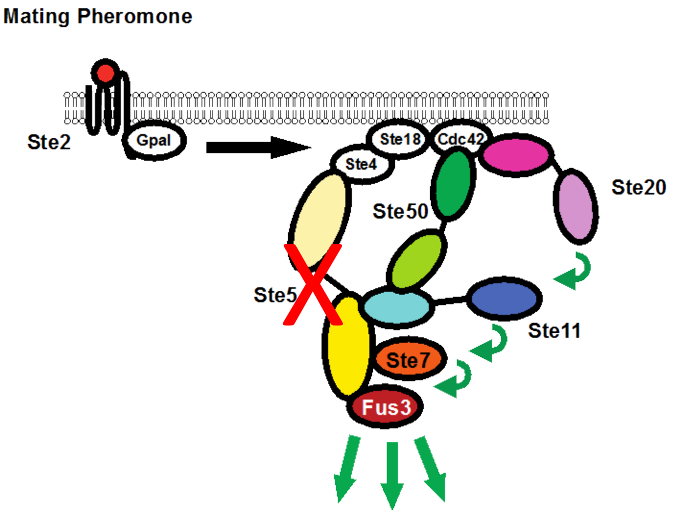
Network re-wiring in the absence of the Ste11 kinase



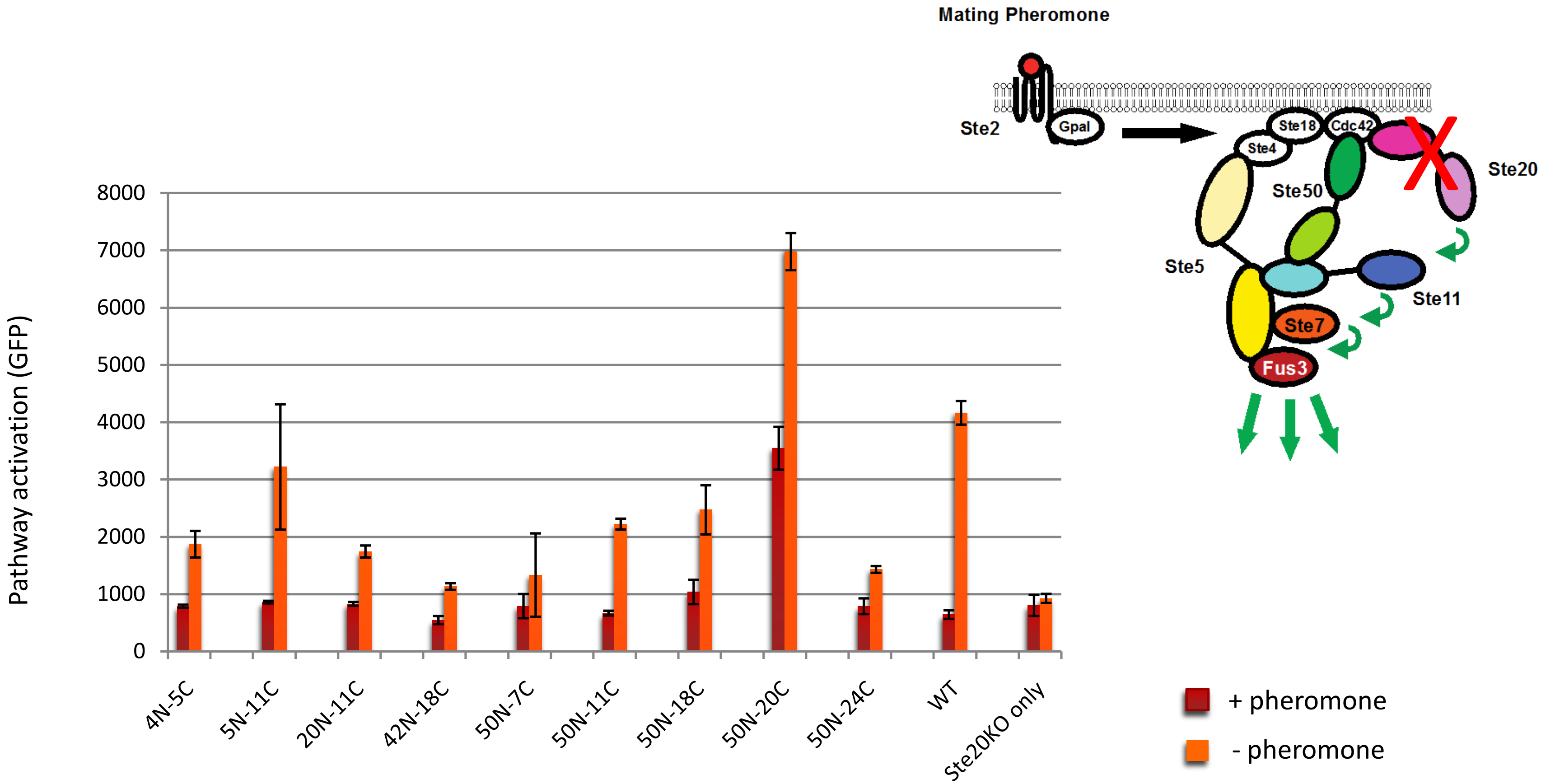


Network re-wiring in the absence of the Ste5 scaffold

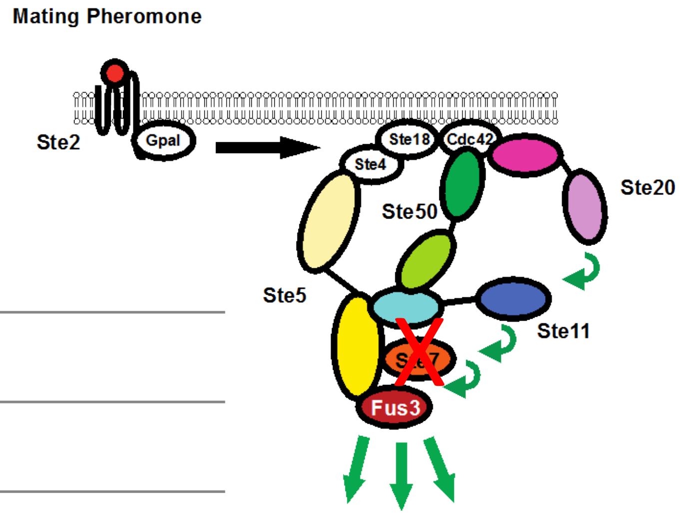


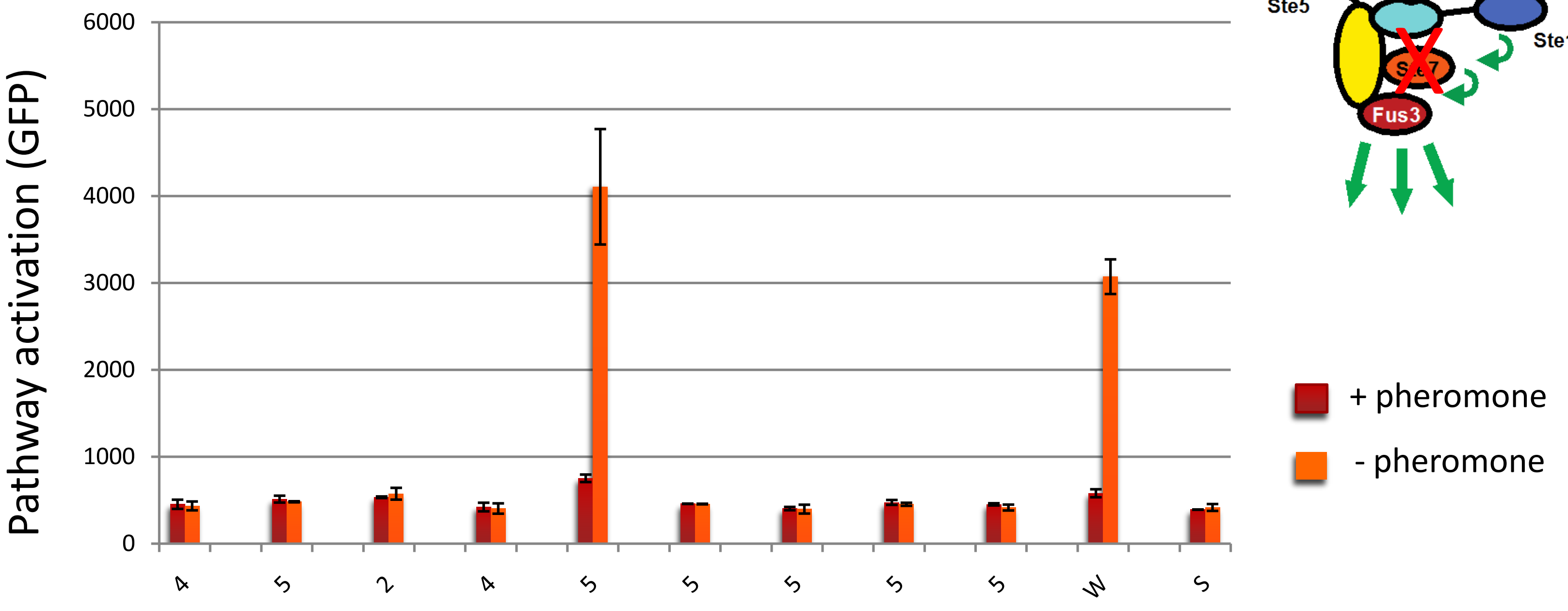


Network re-wiring in the absence of the Ste20 kinase



Network re-wiring in the absence of the Ste7 kinase





Conclusions

• Recombination of modular protein domains leads to the rapid diversification of signaling pathways.

• While domain duplication could lead to dominant negative effects, recombination is needed to create novel pathway responses.

• Most significant changes result from recombination events that alter the localization and/or regulation of catalytic domains.

•Mating network is very plastic, tolerating recombination events that involve deletions of WT genes.

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