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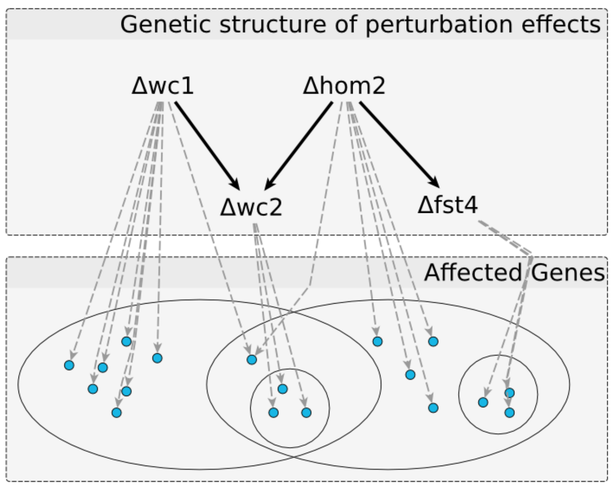
Problem

The Dutch mushroom industry represents 25% of the EU's mushroom production. Due to increased competition from abroad, there has been a push to understand the growth of mushrooms in order to remain competitive.

Mushroom formation is a poorly understood process. We wish to be able to control the formation of mushrooms such that we can control when and where the mushrooms form.

We wish to identify genes which are required for mushroom formation; genes which produce mushrooms when activated.

Finding a genetic hierarchy



Each gene knockout perturbs the expression of a set of genes. Different knockouts result in different sets of genes, but there might be overlap between the sets. Insight into these overlaps give important clues on how knockouts might influence each other. This can be captured by a hierarchical description of the set of perturbed genes as a results of the different knockouts. We wish to infer this kind of relationship between currently studied genes, and new genes.

Nested Effect Models

NEMs [2,3] can be used to inter such structures from expression data, but generally they only work on one dimension, the expression levels. We have to consider two more; time, and phenotype.

The target: *Agaricus bisporus*

Agaricus bisporus, also known as the champignon or the white button mushroom, is one of the most widely cultivated and consumed mushrooms in the world. Other strains of this mushroom are also very valuable as a source of food, such as the chestnut and portobello mushrooms.

Unfortunately, the study of this mushroom is severely hampered by an inability to study it in the laboratory.

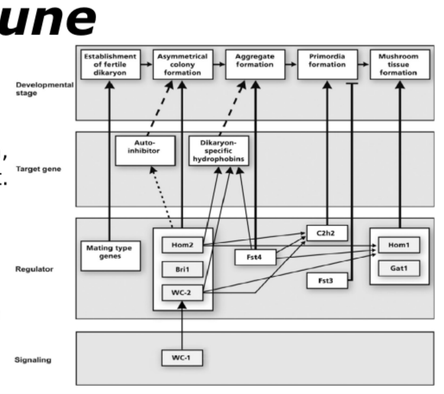
As methods to study *Agaricus bisporus* in the laboratory are still being developed, we have to use a different mushroom as a model for mushroom fruitification.

Schizophyllum commune is the mushroom chosen for this purpose.

A model: *Schizophyllum commune*

Schizophyllum commune is a mushroom consumed widely in Central/Southern America and Asia, but considered inedible in the west.

Conventional biology has characterized a handful of transcription factors which are involved with mushroom formation [1].



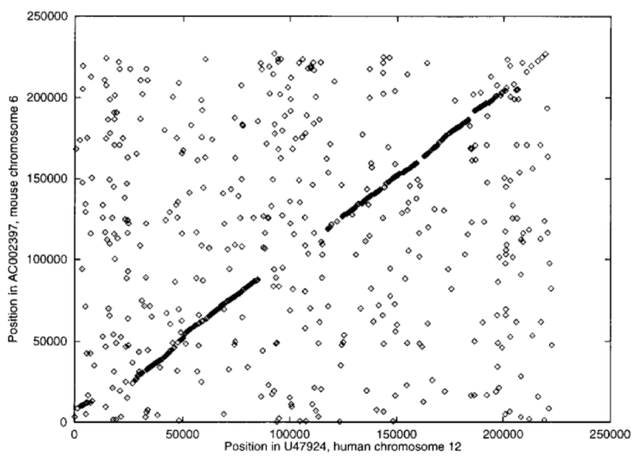
Does the model organism make sense?

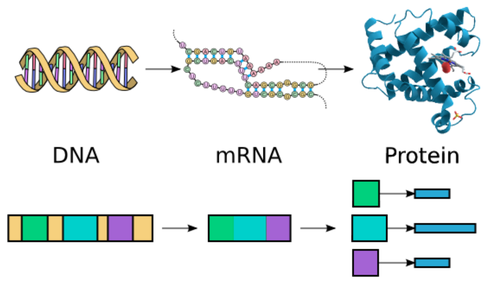
Comparing genomes

The traditional method of comparing genomes is to align the genomes. In the alignment one will identify long diagonal stretches. These regions are highly conserved.

Co-conserved regions within or between genomes are called 'syntenic', and can be used to describe the evolution of a given region.

To the right is presented the example of a human chromosome aligned to a mouse chromosome [4]. These chromosomes share some very strongly syntenic regions.





It is not possible to make a similar plot for our two mushrooms from the DNA. This is because the DNA is not conserved. However, the protein sequences are.

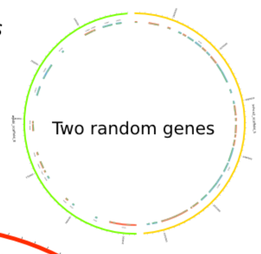
This is possible because multiple combinations of DNA sequences result in the same protein sequence.

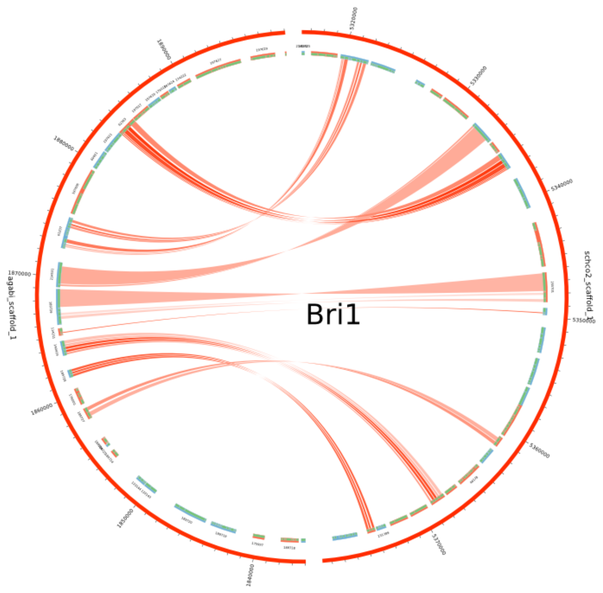
Therefore, we must instead perform our alignments on the ***translated* DNA sequences**.

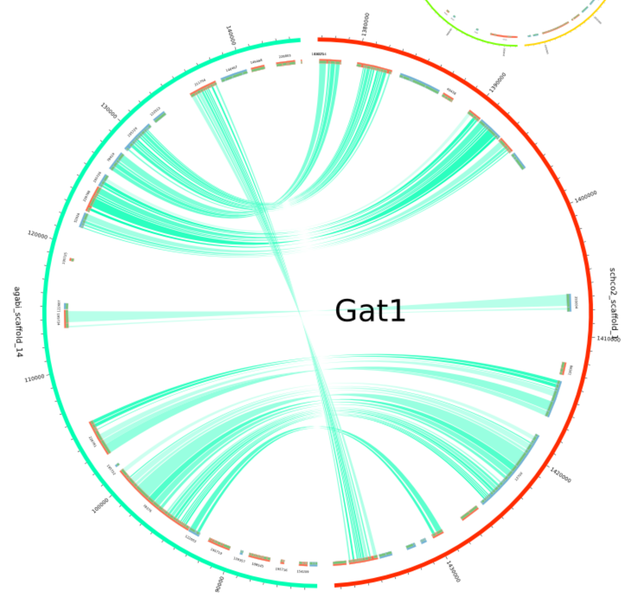
There are similarities at the multi-gene level

By examining the regions surrounding genes of particular interest and their predicted homolog, we can make an attempt at describing the evolution of the genome of *A. bisporus* relative to *S. commune*.

We observe that the genes which we have identified as major players in mushroom formation exist in regions which are conserved between our organisms. Two random genes are rarely observed in a conserved region.



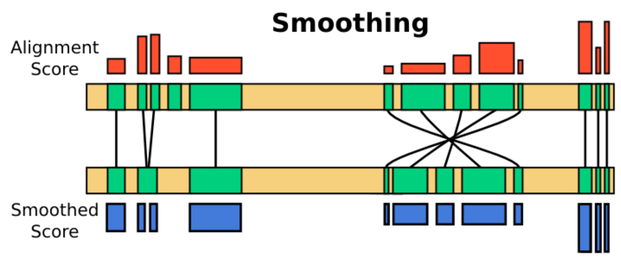


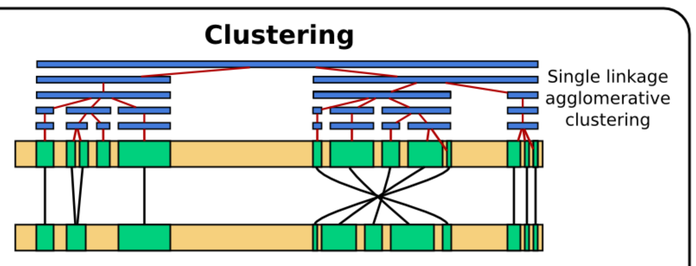


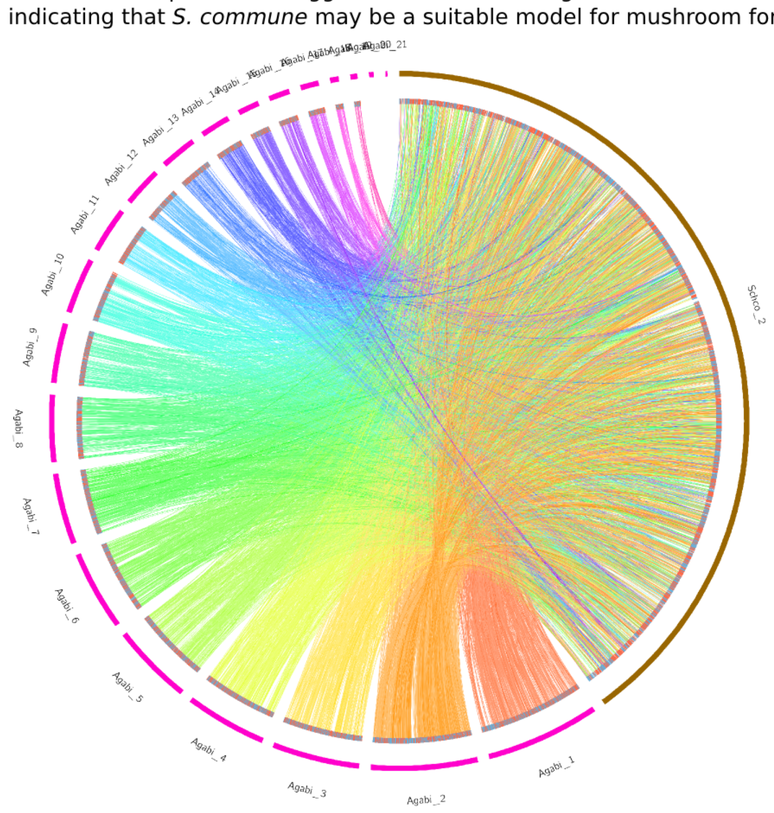
There are similarities at the chromosome level

Looking at all alignments between chromosomes results in a very messy picture (bottom left). There is too much noise. To remove noise, we perform a sliding window smoothing around alignments, to get an overview of alignment quality, and a clustering, to group high quality regions together.

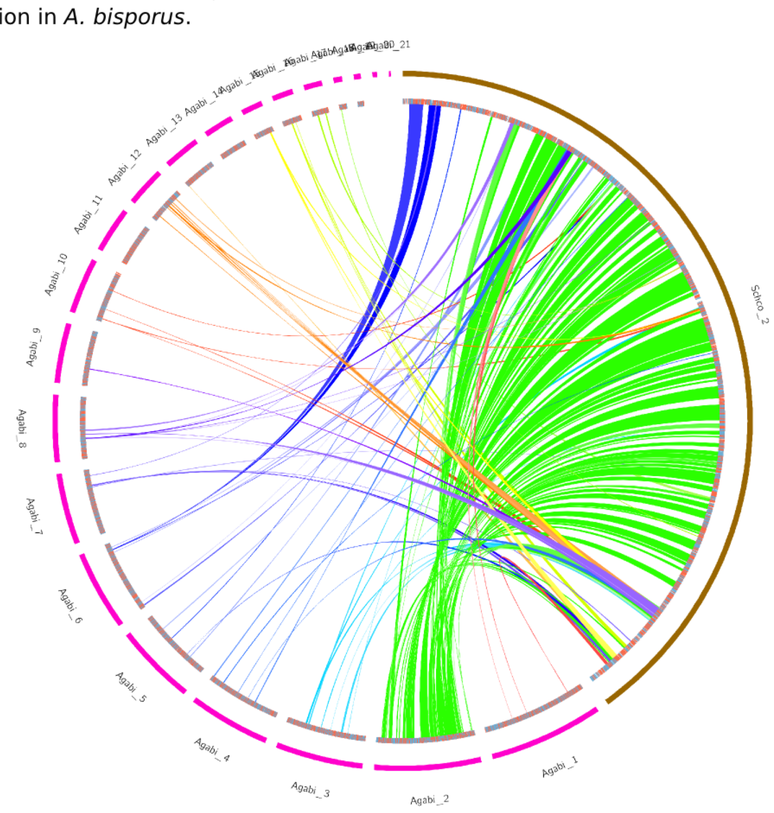
The relationships we see suggest that there are large similarities between the two mushrooms, indicating that *S. commune* may be a suitable model for mushroom formation in *A. bisporus*.



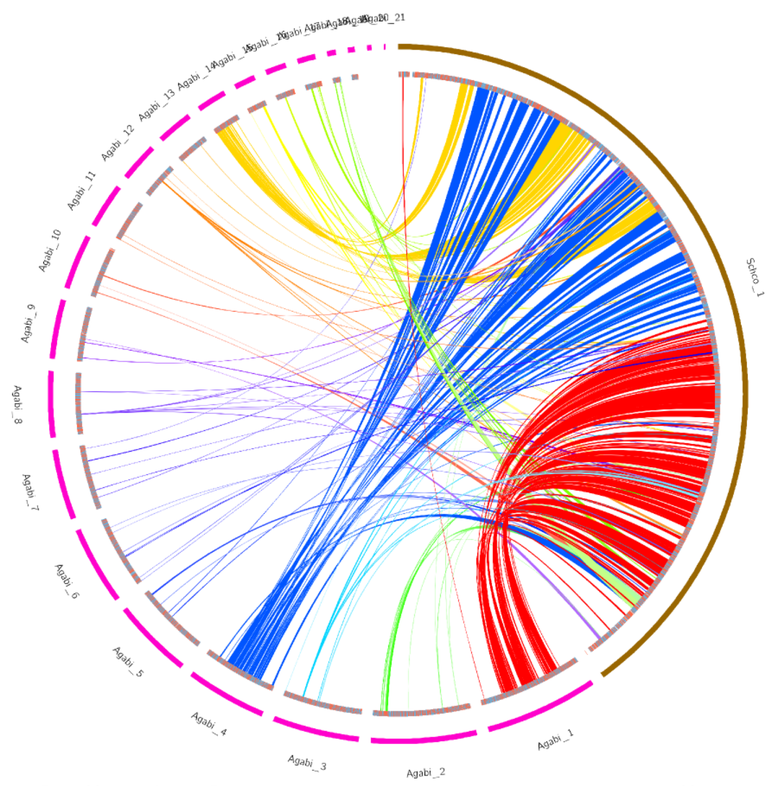




Considering all alignments individually, there is too much noise to get a clear view of the evolution.



Scaffold 2 in *A. bisporus* corresponds (mostly) to scaffold 2 in *S. commune*.



Scaffold 1 in S. commune corresponds to three different scaffolds in A. bisporus.

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