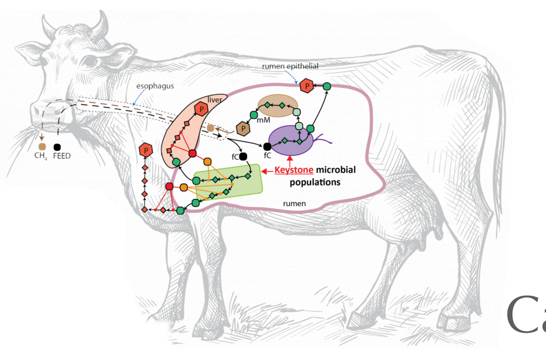

Host-Microbiome Holo-Omics

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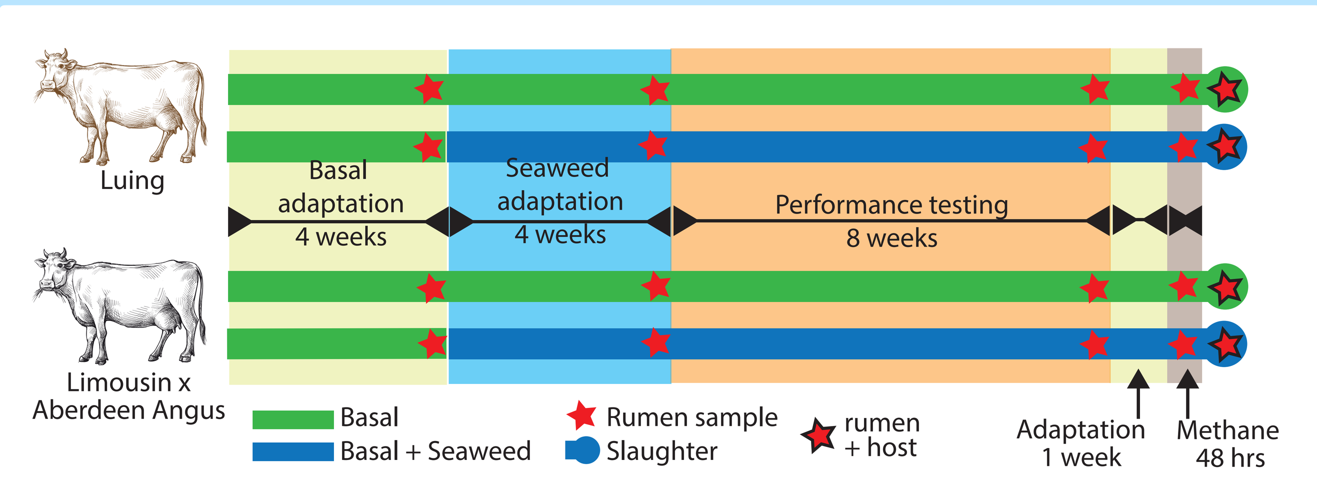
Motivation

The development of high tech sequencing methods now makes it possible to investigate each step of the central bio-molecular dogma (DNA→RNA→Protein→Metabolite) in a host-microbiome context. By combining these molecular layers bioinformatically and contrasting them to a perturbation of the ecological niche in question (herbivore rumen) we will be able to observe and predict host-microbiome interactions from a holistic point of view. This will create new hypotheses to target more specifically in future experiments.

Perturbation of The Rumen Microbiome

Seaweed *Asparagopsis taxiformis* contains halogenic compounds (e.g. $CHBr_3$ aka. bromoform) which effectively inhibits methanogenic archaea. This inflicts a metabolic shift which affects the microbial composition in the rumen of the cattle.

Red algae seaweed
Asparagopsis taxiformis



In this trial, a total of 80 cattle were monitored temporally on 2 contrasting diets, with 40 eating a basal control feed and 40 eating an *Asparagopsis taxiformis* supplemented feed. Tissue from organs related to digestion were collected at slaughter: Rumen Wall, Liver, Lung, Kidney, Adrenal gland and Spleen.

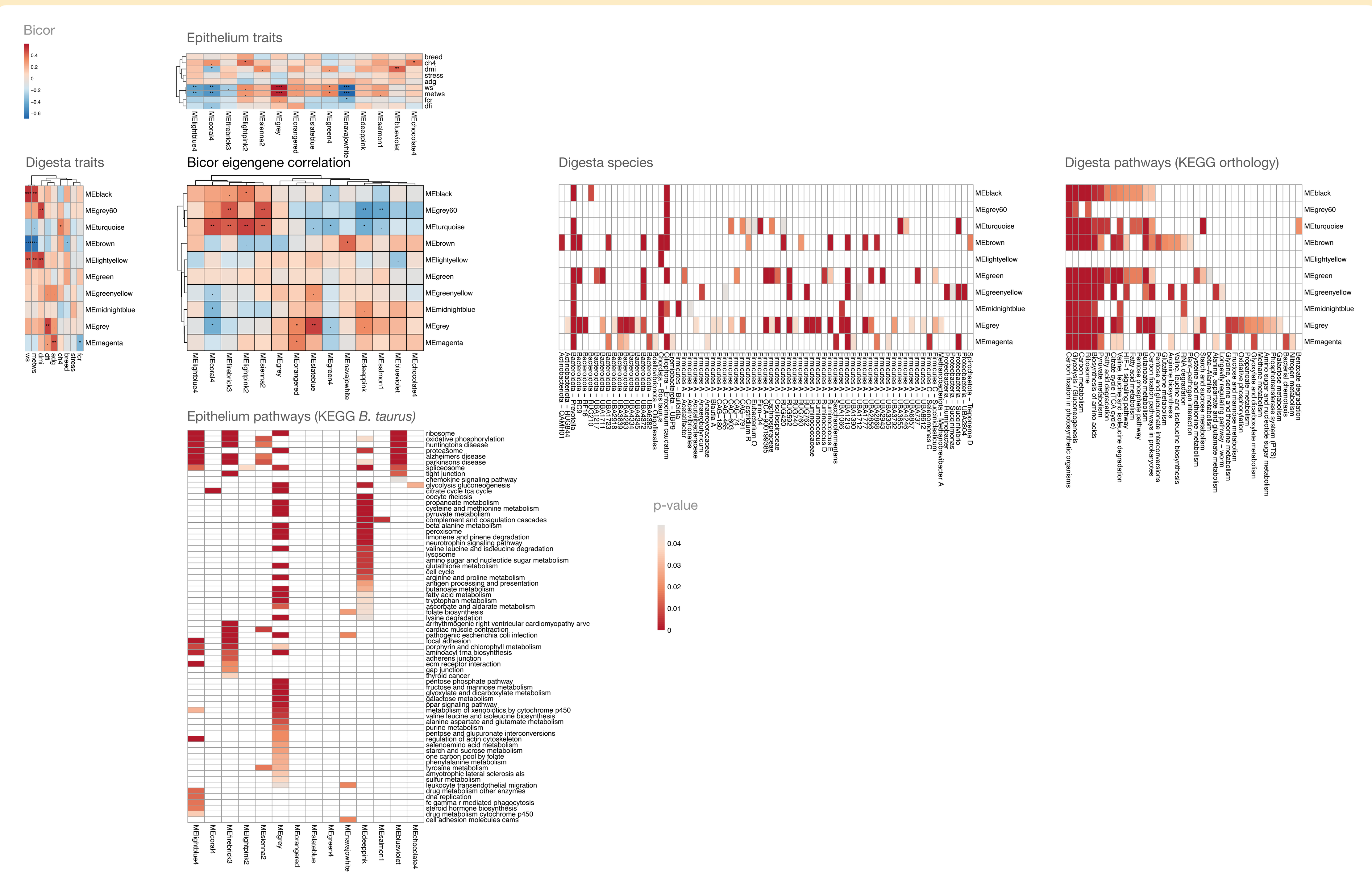
Generating a Multi-Omics Data Set

We sequenced each molecular layer of both the host and the microbiome of the rumen. Given the contrasting samples, we had to resort to many different technologies in order to completely cover the biology of the host-microbiome interaction.

←← Molecular Layer →→		←←← Microbiome/Host Sample Source →→→		
		Digesta fluid from rumen (microbial soup)	Epithelium of the rumen (host)	Liver (host)
	DNA *Genomics*	16S for diversity illumina for depth (0.5E9 reads) Nanopore for length (480 Gbp ONT-R10)	SNP-genotyping (including parental genotypes)	
	RNA *Transcriptomics*	illumina (1.2E9 reads)	illumina (1.2E9 reads)	illumina (1.2E9 reads)
	Protein *Proteomics*	LC-MS/MS (targets from corresponding MAGs)	LC-MS/MS (targets from host genome)	LC-MS/MS (targets from host genome)
	Volatile Fatty Acid (VFA) *Metabolomics*	Targeted VFA analysis (6 VFA targets)		
	Untargeted Non-Protein *Metabolomics*	LC-MS/MS (62 targets)	LC-MS/MS (62 targets)	LC-MS/MS (62 targets)
	Plant Fibre *Metabolomics*	Microarray Polymer Profiling (48 probes)		
	Key Performance Indices	Methane production (CH_4) Average daily gain (ADG) Feed Conversion Ratio (FCR)		

Integrating Proteomics from Host and Microbiome

Weighted Gene Co-expression Network Analysis (WGCNA) is an algorithm that makes use of hierarchical clustering and topological overlap measure (TOM) in order to group each expression unit (gene or protein) into functional clusters represented by eigengenes. These eigengenes are then correlated between two independent sample sources that interact biologically (host and microbiome). Below we present an example from a metaproteomics analysis that was generated from both rumen fluid (digesta) and rumen wall tissue (epithelium) from 36 cattle.



Here, as a means of testing of our approach, we grouped the proteins from the rumen microbial fluid (digesta) and proteins from the rumen wall (epithelium) independently into eigengene groups with WGCNA. By cross correlating the eigengenes between the microbes and the host, we're able to see which functional groups of proteins interact within the host-microbiome interface.

My name is Carl and I'm doing a PhD in The MEMO group at NMBU. Reach out to me at: carl.mathias.kobel@nmbu.no

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Noregs miljø- og biovitskaplege universitet

SRUC

novo nordisk fonden

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