The optimization problems of rumen microbes

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Modélisation Systémique Appliquée aux Ruminants

Ultimate goal

To develop the knowledge, and tools, that allow an **optimal balance** to be found between performance, robustness functions and animal well-being, and thereby an improved efficiency of use of feed resources

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Who

- Interdisciplinary research team (16): Physiologists, Nutritionists, Ethologists, Modellers
- Team director: Nicolas Friggens
- Animal model: goat
- Location: Paris (AgroParisTech) & Thiverval-Grignon (Farm with 100 goats)

Our interest to participate in MOABI?

Perspective of an user

- Identify robust optimization tools adapted to our research questions
- Identify potential collaborations

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Plan

- Describe (briefly) our research topic
- Indicate our needs for optimization tools

Ruminants & Humans: a prehistoric relationship that contributed to the human conquer of hostile lands

Prehistoric, and often nomadic, hunters realized that they could exploit the photosynthetic potential of grasslands by domesticating ruminants, and subsequent increases in food supply allowed them to form stable social communities.

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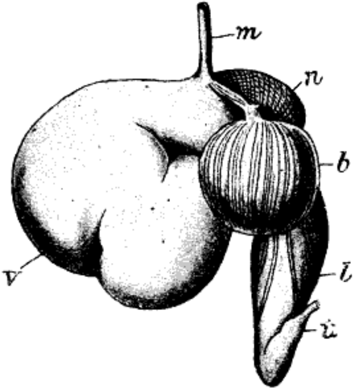
The rumen & its microbes



m. oesophagus
v. rumen
n. reticulum
b. omasum
l. abomasum
t. beginning of the intestine

Source wikipedia

The rumen & its microbes

- Rumen: anaerobic compartment, central organ where the main responses to feeding practices are produced
- Microbial community (10^{11}cells/mL): hundreds of species (Bacteria, Archaea, Protozoa, and Fungi)

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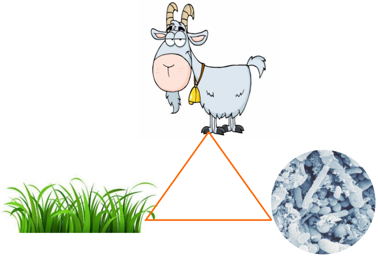
Fermentation of dietary polymers by rumen microbes produces:

- Energetic compounds for the animal ☺
- Microbial biomass (rich protein source for the host) ☺
- Methane: potent greenhouse gas ☹

The rumen & its microbes

Our goal

Understand the role of rumen function on the adaptation and robustness of the animal via a mathematical modelling approach



Scientific questions

- What is the role of **thermodynamics** on rumen fermentation?
- What is the role of the **microbiota** on the **interindividual variability**?
- What is the role of the microbiota on rumen **robustness** and animal robustness?
- How to drive rumen fermentation to **maximize animal** performance in a **sustainable** manner?

Mathematical approaches

1. Macroscopic kinetic models: ordinary differential equations
    - Existing rumen models: (Baldwin et al 1987, Dijkstra et al 1992, Lescoat & Sauvant 1995, Vetharaniam et al 2015)
    - Our approach: based on anaerobic digestion models for:
        - ⋆ Engineering reactors (Batstone et al 2002)
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2. Genome-scale metabolic models for microbial communities
   - Flux balance analysis (Varma&Palsson 1993, Lewis et al 2012)
   - Resource Balance Analysis (Goelzer et al 2011)

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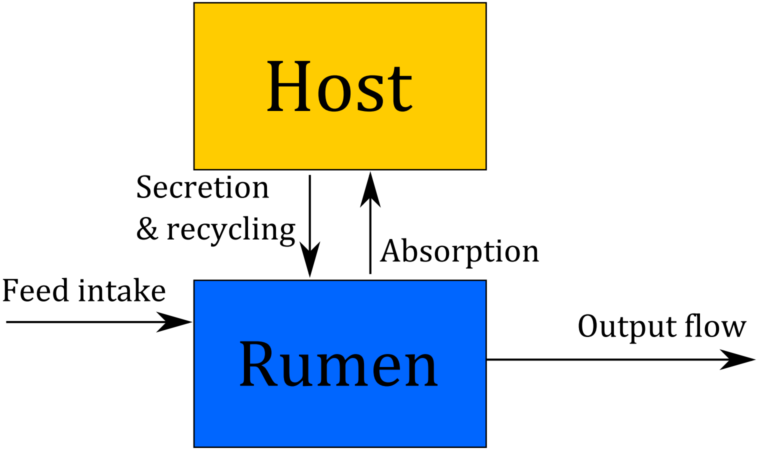
Mathematical modelling of *in vitro* fermentation



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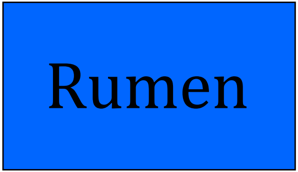


Mathematical modelling of *in vitro* fermentation

$$\frac{\mathrm{d}\boldsymbol{c}}{\mathrm{d}t} = \mathbf{S} \cdot \boldsymbol{r}(\boldsymbol{c}, \boldsymbol{p}) + \boldsymbol{g}(\boldsymbol{c}, \boldsymbol{p}) \qquad (1)$$

- $\mathbf{S} \cdot \boldsymbol{r}(\boldsymbol{c}, \boldsymbol{p})$: biological phenomena → microbial fermentation
- $\boldsymbol{g}(\boldsymbol{c}, \boldsymbol{p})$: physico-chemical phenomena → acid-base reactions, liquid-gas transfer

$\boldsymbol{c}$: **18** state variables

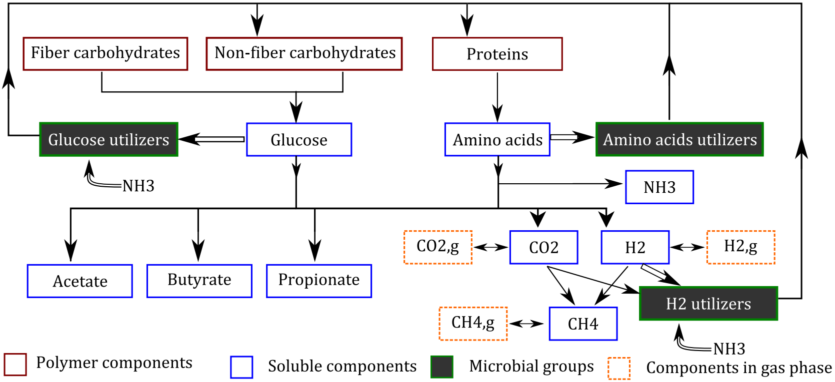
$\boldsymbol{p}$: **30** parameters

⋆ Reduction via stoichiometric relationships

⋆ **12** parameters to be estimated (sensitivity analysis from literature)

Stiff model: slow processes (polymer breakdown, τ days), instantaneous process (acid-base reactions)

Mathematical modelling of *in vitro* fermentation



Acid-base equilibrium reactions are included for pH determination

Model calibration with data from two experiments

- Experimental data from Serment et al 2016
- Matlab IDEAS Toolbox (Muñoz-Tamayo et al 2009)
  freely available at
  http://www.inra.fr/miaj/public/logiciels/ideas/index.html
  - Maximum likelihood estimator
  - Allows different hypothesis on the covariance matrix (Gaussian measurement errors)
  - Symbolic derivation of sensitivity functions
  - Local optimization using Nelder-Mead Simplex method (Lagarias et al., 1998)

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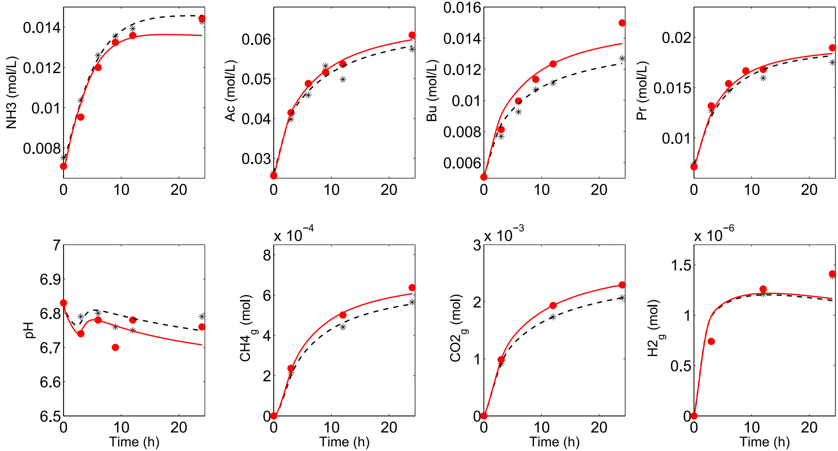

Muñoz-Tamayo et al. Under review in Animal Feed Science and Technology

Prospects

- Incorporate physiological aspects (*in vivo*)
- Incoporate thermodynamic control
- Account for interindividual variability: fast vs slow eaters, high vs low buffer capacity
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$\Downarrow$

Increase of model complexity: state variables & parameters

Adapted optimization tools for:

- Parameter estimation for large-scale models
- Optimal experiment design: protocol **P**

$$\min_{\mathsf{P}} \; J(\sigma_i), \; i = 1, \ldots, n_{\mathsf{p}} \qquad (2)$$

  - Constraints of animal experimentation: sampling time, accessibility
  - Legislation on animal care (**R**educe, **R**efine, **R**eplace)

Adapted optimization tools for:

- Design of optimal nutritional strategies
  - Optimizing animal performance: multiobjective, mixed-integer dynamic optimization problem (feed composition, feed frequency)

    max milk (meat) production

    max animal welfare

    max animal robustness

    max economic profit

    min risk physiological states (acidosis)

    min carbon (energy) lost

    min methane emissions

Thanks

Questions & comments

In vitro experimental study

Treatments:

- Level of concentrate in the substrate (L_s, H_s)
- Rumen inocula adapted to high or low concentrate diet (L_i, $H_i s$)
- 2×2 factorial design

Measurements:

- Acetate, butyrate, propionate
- NH_3
- Gas components: CO_2, H_2, CH_4
- pH