Construction of a Machine Learning tool based on Differential Equations integrated into a dynamic tree allowing biological data assimilation

Harold Moundoyi, Marouan Handa, Thi Vo
Nicolas Bloyet, Hélène Flourent, Emmanuel Frénod

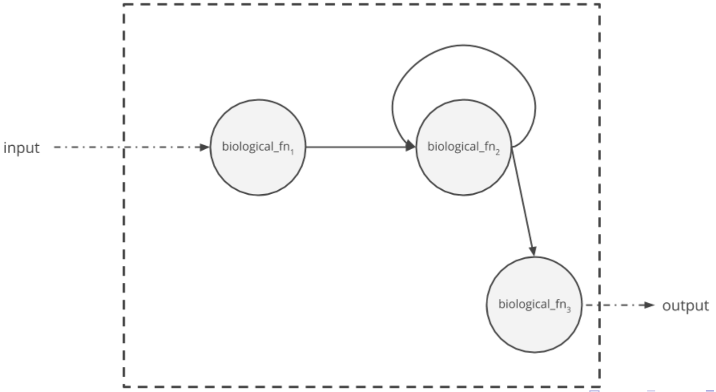
CEMRACS 2018

23 August 2018

- Modeling of the digestive behaviour
- The goal: build Machine Learning algorithms based on the discretization of Differential Equations in order to predict biological responses and assimilate biological data.

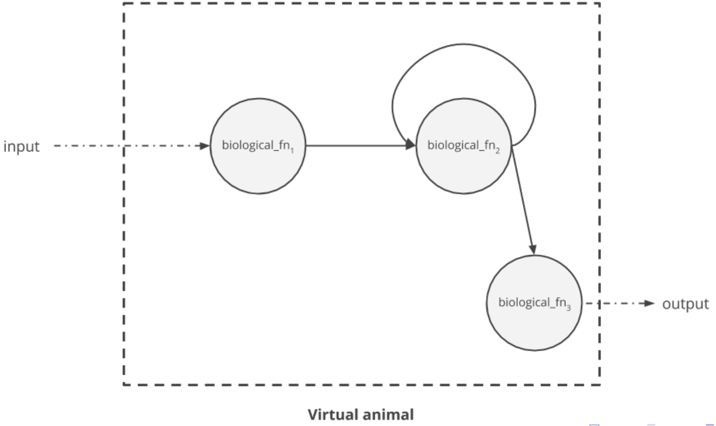
Graph-oriented Model

- The main idea: Assimilate an animal to a graph in which nodes are virtual organs and edges represent fluxes within the organism.



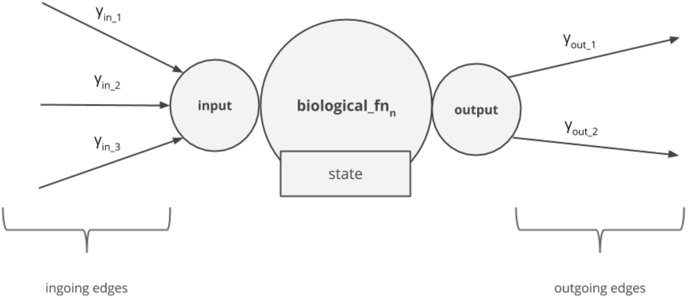
Graph-oriented Model

- Each virtual organ carry a biological function, which aimed to reproduce at best its actual behaviour.



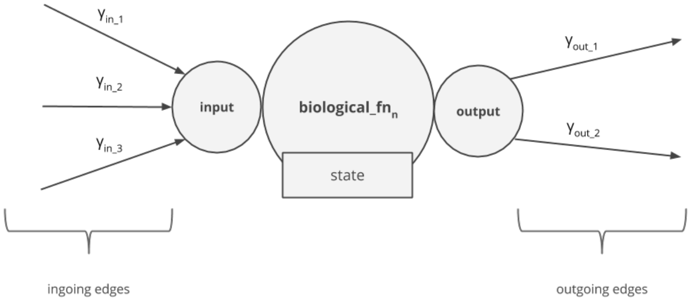
Graph-oriented Model

- Each link is weighted with a parameter γ_i, on which indicates how inputs and outputs are actually dispatched, and to give more or less significance on links between organs.



Graph-oriented Model

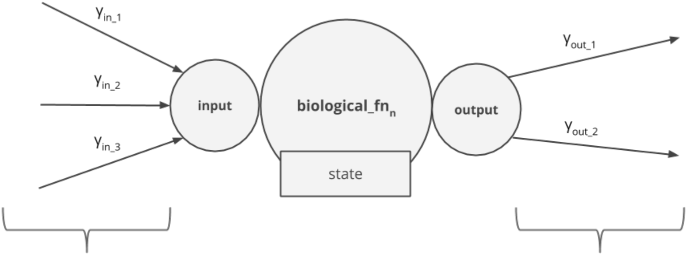
- Each node (organ) is given some memory, which are states. They can thus store and use several values, which can be part of their function definition.



Graph-oriented Model

The process of such function is as follows:

1) Aggregate all the ingoing fluxes coming from other functions
2) Given those inputs, compute the function output for this time step.
3) Propagate the computed output to all outgoing edges.



Global Optimization

Optimize the whole animal in order to find the parameters values that would make it fit at best the real data.

2 approaches:

1) Analytic approach: Analytically resolve the functions, by fixing some parameters each by each.

Global Optimization

Optimize the whole animal in order to find the parameters values that would make it fit at best the real data.

2 approaches:

1) Analytic approach: Analytically resolve the functions, by fixing some parameters each by each.
2) Machine Learning approach: Optimization (Genetic optimization methods, Least square method...)
$\Longrightarrow$ Fast to implement.

Applied case: Ross Chicken growth

ROSS 708

http://en.aviagen.com/brands/ross/products/ross-708

Applied case: Ross Chicken growth

Some information on those animals are available, for each sex of the strains:
-Daily consumption of food.
-Daily growth (Weight).

ROSS 708

http://en.aviagen.com/brands/ross/products/ross-708

ROSS 708

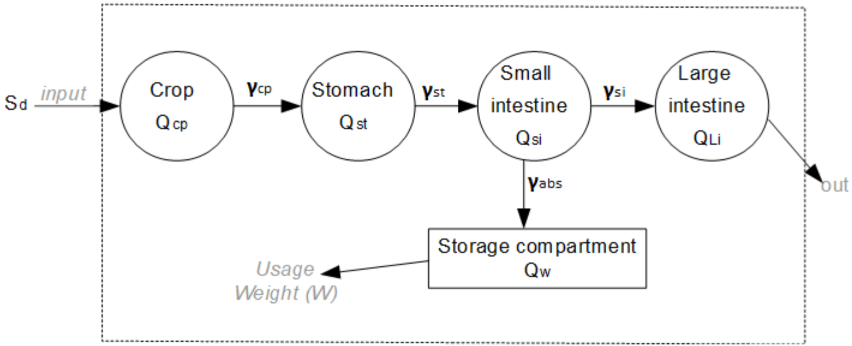
http://en.aviagen.com/brands/ross/products/ross-708

- At first, we consider the growth(mass gained each day) .
- Flux to consider is the food consumption which becomes later a nutrients flux.

Recall of some growth functions

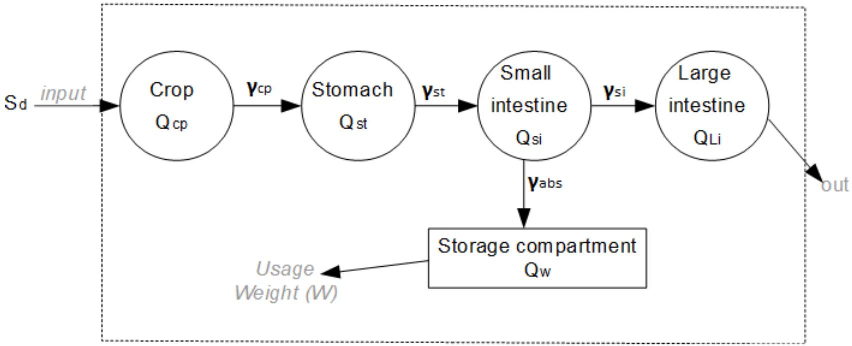
- Logistic: $W' = \mu_0 W \left(1 - \frac{W}{W_f}\right)$
- Gompertz: $W' = DW \ln\left(\frac{W_f}{W}\right)$
- Richards: $W' = DW \left(\frac{W_f^n - W^n}{nW_f^n}\right)$

Assumptions



A1 Ingested food is stored in the crop before moving into the stomach.

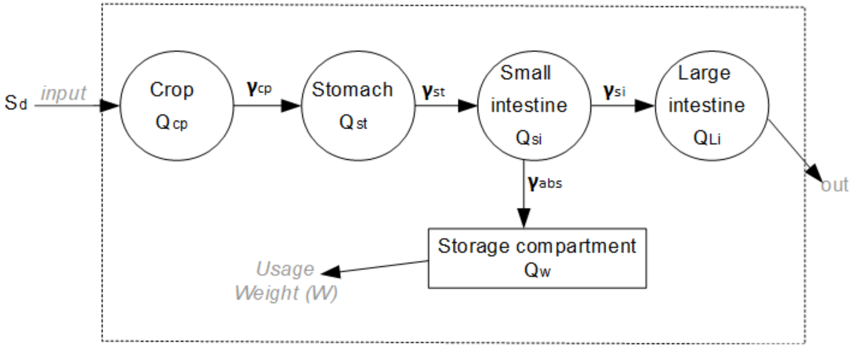
Assumptions



A1 Ingested food is stored in the crop before moving into the stomach.

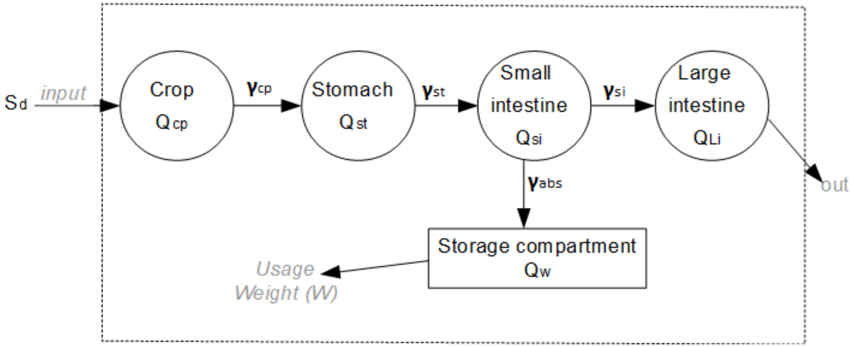
A2 Some fluxes rates are constant between compartements.

Assumptions



A3 Existence of transmission delays in some compartments.

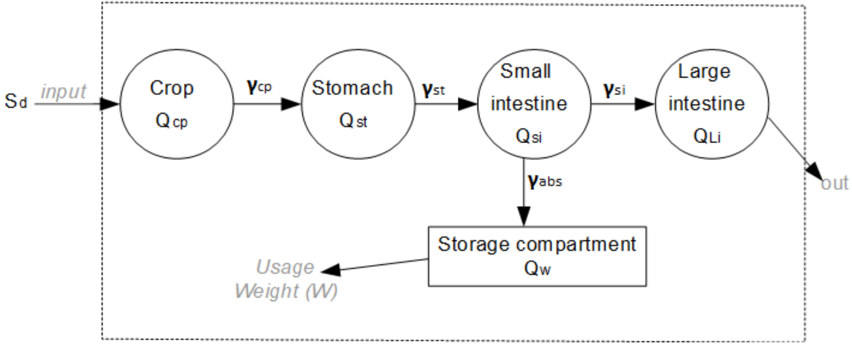
Assumptions



A3 Existence of transmission delays in some compartments.

A4 There exists a time τ for which the SI empting dynamic starts.

Equations

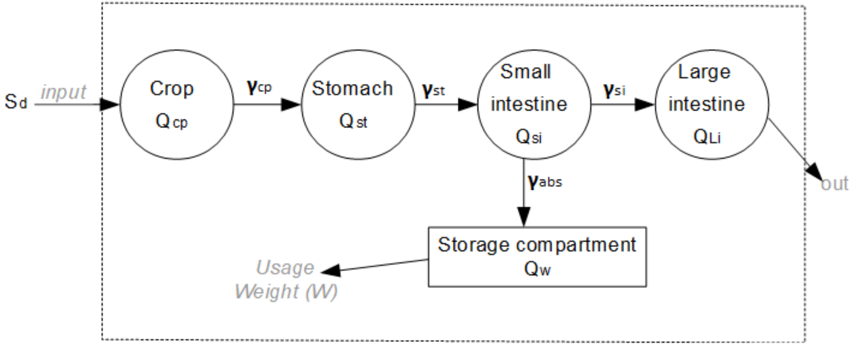


Crop

$$Q'_{cp,d} = -\gamma_{cp} Q_{cp,d}$$

$$Q_{cd,d}(0) = S_d$$

Equations

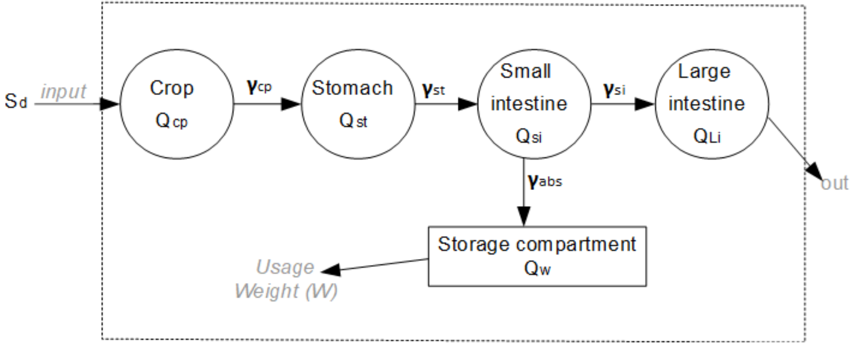


Stomach

$$Q'_{st,d} = \gamma_{cp} \left(1 - \exp(-\beta_1 t)\right) Q_{cp,d} - \gamma_{st} Q_{st,d}$$

$$Q_{st,d}(0) = 0.$$

Equations

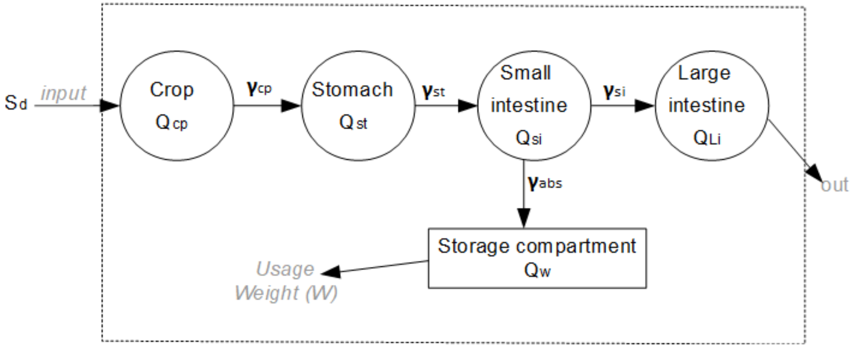


Small intestine

$$Q'_{si,d} = \begin{cases} \gamma_{st} Q_{st,d}, & t \leq \tau \\ \gamma_{st} Q_{st,d} - (\gamma_{abs} + \gamma_{si}) Q_{si,d}, & t > \tau \end{cases}$$

$$Q_{si,d}(0) = 0.$$

Equations



Large intestine

$$Q'_{Li,d} = \gamma_{si} Q_{Li,d} - \gamma_{Li} Q_{Li,d}$$
$$Q_{Li,d}(0) = 0.$$

Equations

Storage and usage of nutrients

$$Q'_{w,d} = \gamma_{abs} Q_{si,d} - \alpha Q_{w,d}$$
$$Q_{w,d}(0) = Q_{w,d-1}$$

Equations

Storage and usage of nutrients

$$Q'_{w,d} = \gamma_{abs} Q_{si,d} - \alpha Q_{w,d}$$
$$Q_{w,d}(0) = Q_{w,d-1}$$

A6 Anabolism prevailing over catabolism (Pütter 1920).

Equations

Storage and usage of nutrients

$$Q'_{w,d} = \gamma_{abs} Q_{si,d} - \alpha Q_{w,d}$$
$$Q_{w,d}(0) = Q_{w,d-1}$$

A6 Anabolism prevailing over catabolism (Pütter 1920).

Formation of the daily weight

$$W'_d = \kappa(t) Q_{w,d} - \left(V_{max} \frac{Q_{w,d}}{K + Q_{w,d}} \right) \frac{1}{K} W_d$$
$$W_d(0) = 0.$$

Equations

Storage and usage of nutrients

$$Q'_{w,d} = \gamma_{abs} Q_{si,d} - \alpha Q_{w,d}$$
$$Q_{w,d}(0) = Q_{w,d-1}$$

A6 Anabolism prevailing over catabolism (Pütter 1920).

Formation of the daily weight

$$W'_d = \kappa(t) Q_{w,d} - \left(V_{max} \frac{Q_{w,d}}{K+Q_{w,d}}\right) \frac{1}{K} W_d$$
$$W_d(0) = 0.$$

A7 $$\begin{cases} \kappa' = -\mu\kappa \\ \mu' = \beta_2(\mu_{max} - \mu) \end{cases}$$

Equations

Formation of the daily weight

$$W_d' = \kappa(t) Q_{w,d} - \left(V_{max} \frac{Q_{w,d}}{K + Q_{w,d}} \right) \frac{1}{K} W_d$$

$$W_d(0) = 0.$$

A7 $$\begin{cases} \kappa' = -\mu\kappa \\ \mu' = \beta_2(\mu_{max} - \mu) \end{cases}$$

$$\Longrightarrow \kappa(t) = \kappa_0 \exp\left[-\mu_{max} \left(t - \frac{1 - \exp(-\beta_2 t)}{\beta_2} \right) \right]$$

Equations

Formation of the daily weight

$$W_d' = \kappa(t) Q_{w,d} - \left(V_{max} \frac{Q_{w,d}}{K+Q_{w,d}} \right) \frac{1}{K} W_d$$

$$W_d(0) = 0.$$

A7 $\begin{cases} \kappa' = -\mu\kappa \\ \mu' = \beta_2(\mu_{max} - \mu) \end{cases}$

$$\Longrightarrow \kappa(t) = \kappa_0 \exp\left[-\mu_{max} \left(t - \frac{1-\exp(-\beta_2 t)}{\beta_2} \right) \right]$$

Final weight $W_f = W_0 + \sum_{d=1}^{N_d} W_d(t_f)$

N_d: number of days.

Simulations

- Observed data
  - Daily feed intake.
  - Daily weight measurement.
- Discretization: FDM(Forwards Euler method);
- fitting: γ_{cp} and τ fixed.

  Estimate $\beta_1, \gamma_{st}, \gamma_{abs}, \gamma_{si}, \gamma_{Li}, \kappa_0, \mu_{max}, \beta_2, V_{max}, K$

Simulations

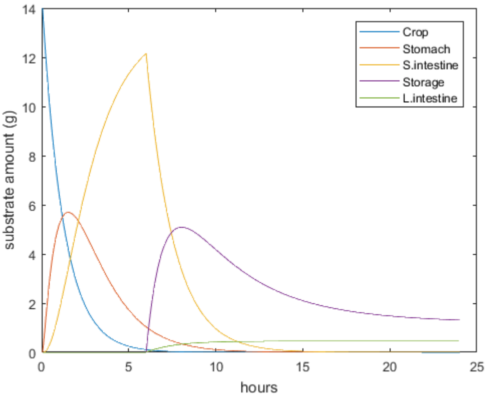


Figure: One day dynamic, $\beta_1 = 0.4, \gamma_{st} = 0.6, \gamma_{abs} = 0.6, \gamma_{si} = 0.023, \kappa_0 = 0.9, \mu_{max} = 0.01, \beta_2 = 0.01, V_{max} = 0.07, K = 26.8$

Simulations

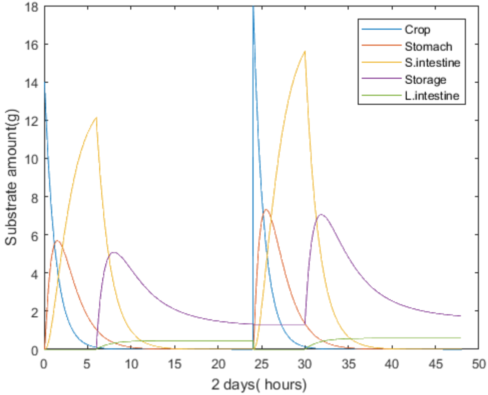


Figure: 2 days dynamic, $\beta_1 = 0.4, \gamma_{st} = 0.6, \gamma_{abs} = 0.6, \gamma_{si} = 0.023, \kappa_0 = 0.9, \mu_{max} = 0.01, \beta_2 = 0.01, V_{max} = 0.07, K = 26.8$

Simulations

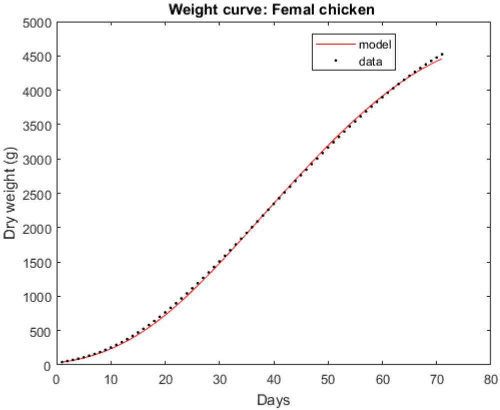


Figure: $\beta_1 = 0.4, \gamma_{st} = 0.6, \gamma_{abs} = 0.6, \gamma_{si} = 0.023, \kappa_0 = 0.9, \mu_{max} = 0.01, \beta_2 = 0.01, V_{max} = 0.07, K = 26.8$

Simulations

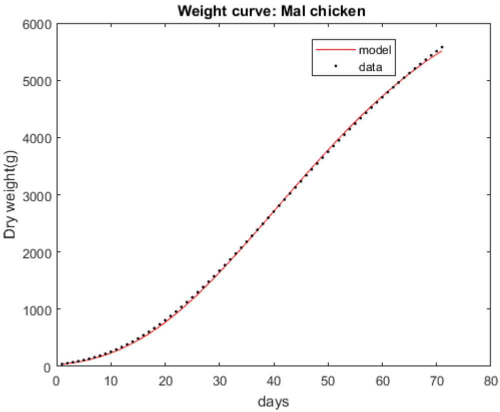
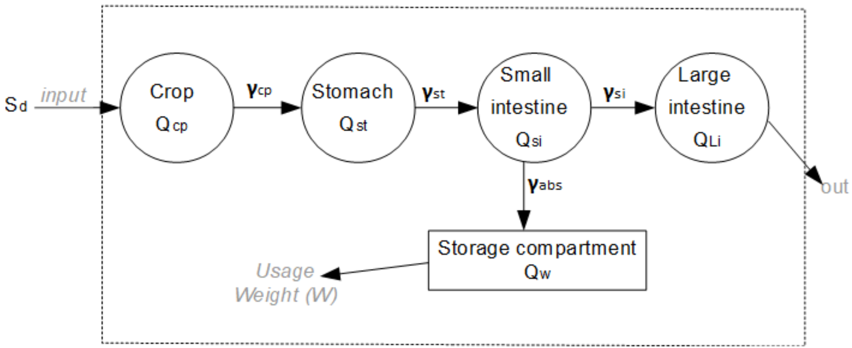
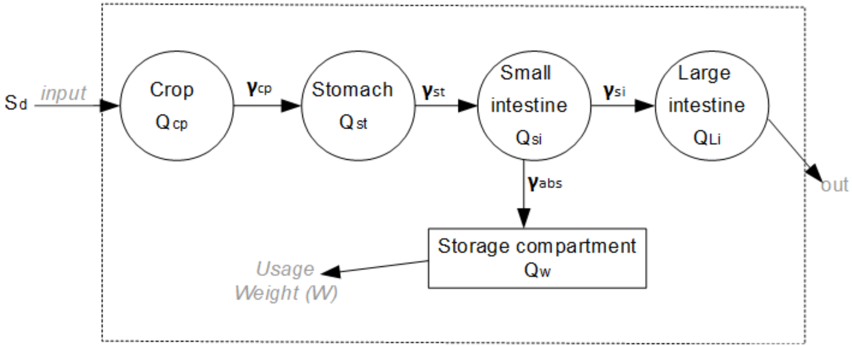
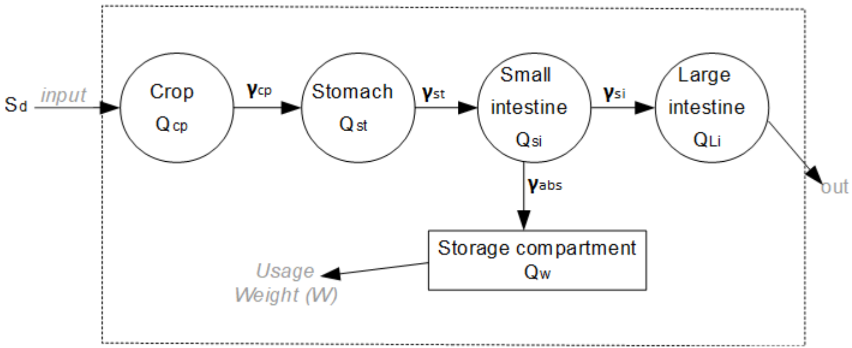


Figure: $\beta_1 = 0.4, \gamma_{st} = 0.6, \gamma_{abs} = 0.6, \gamma_{si} = 0.023, \kappa_0 = 0.9, \mu_{max} = 0.01, \beta_2 = 0.01, V_{max} = 0.07, K = 26.8$


Sd
input
Crop
Qcp
γcp
Stomach
Qst
γst
Small
intestine
Qsi
γsi
Large
intestine
QLi
out
γabs
Storage compartment
Qw
Usage
Weight (W)

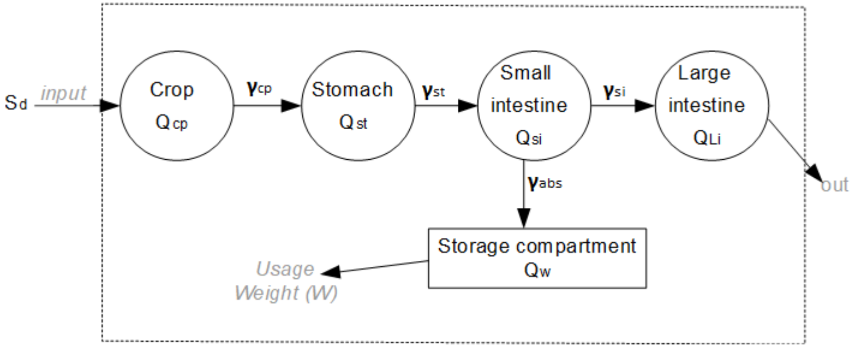


Python code: Virtual chicken.



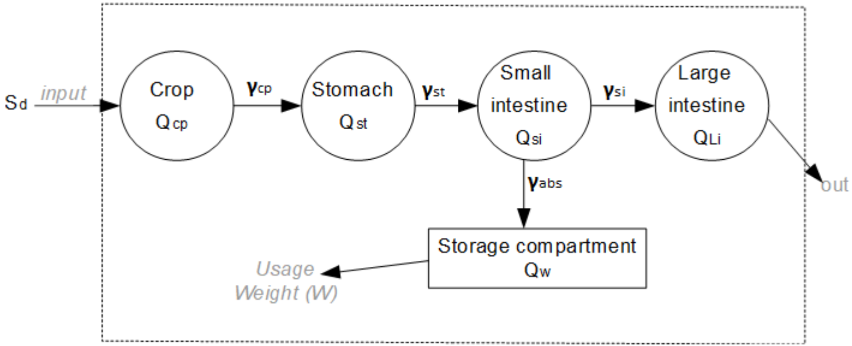
Python code: Virtual chicken.

- Daily food consumption and it composition.



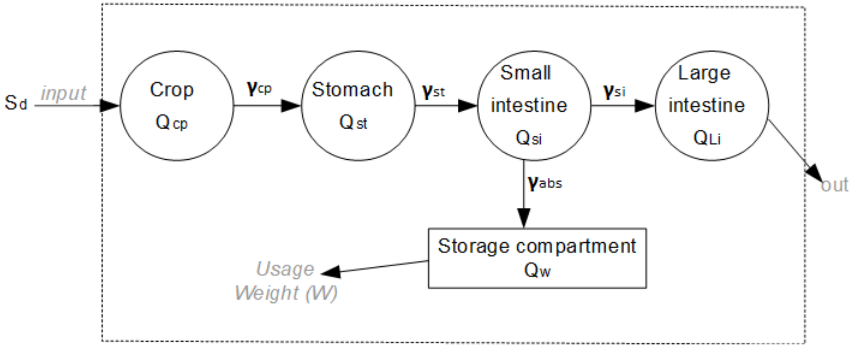
Python code: Virtual chicken.

- Daily food consumption and it composition.
- Mathematical description of biological functions.



Python code: Virtual chicken.

- Daily food consumption and it composition.
- Mathematical description of biological functions.
- Optimize different parameters.



Python code: Virtual chicken.

- Daily food consumption and it composition.
- Mathematical description of biological functions.
- Optimize different parameters.
- Predicts the daily growth.

Challenges and perspectives

- Challenges:

Challenges and perspectives

- Challenges:
  1. No experience on Maching Learning.

Challenges and perspectives

- Challenges:
  1. No experience on Maching Learning.
  2. Not enough documentation.

Challenges and perspectives

- Challenges:
  1. No experience on Maching Learning.
  2. Not enough documentation.
  3. Lack of data concerning:
     Food composition (Nutrients).
     Absorbtion mecanism (active transport, passive diffusion).

Challenges and perspectives

- Challenges:
  1. No experience on Maching Learning.
  2. Not enough documentation.
  3. Lack of data concerning:
     Food composition (Nutrients).
     Absorbtion mecanism (active transport, passive diffusion).
  4. Behaviour of a digestive track:
     Estimation of different fluxes rates.
     Important biological processes happening in different compartments.

Challenges and perspectives

- Challenges:
  1. No experience on Maching Learning.
  2. Not enough documentation.
  3. Lack of data concerning:
     Food composition (Nutrients).
     Absorbtion mecanism (active transport, passive diffusion).
  4. Behaviour of a digestive track:
     Estimation of different fluxes rates.
     Important biological processes happening in different compartments.
- Perspectives:
  1. Find needed DATA in order to build a better descriptive model.

Challenges and perspectives

- Challenges:
  1. No experience on Maching Learning.
  2. Not enough documentation.
  3. Lack of data concerning:
     Food composition (Nutrients).
     Absorbtion mecanism (active transport, passive diffusion).
  4. Behaviour of a digestive track:
     Estimation of different fluxes rates.
     Important biological processes happening in different compartments.
- Perspectives:
  1. Find needed DATA in order to build a better descriptive model.
  2. Build a virtual chicken that allows fitting parameters using Machine Learning approach.

Références

- Sunil S. Jambhekar, Philip J.Breen, Basic pharmacokinetics, second edition, Royal Pharmaceutical Society of Great Britain 2012.
- G.C.Perry. Avian gut function in health and disease, poultry science symposium series volume twenty eight.
- Peter L.Bonate, Pharmacokinetic-Pharmacodynamic modeling and simulation, second edition, Springer science+Business Media, LLC 2011.
- Lawrence X. Yu, Gordon L.Amidon, Compartmental absorbtion and transit model for estimating oral drug absorbtion. International journal of Pharmaceutics 186(1999) 119-125.
- D. Bastianelli, D.Sauvant and A.Rerat, mathematical modeling of digestion and nutrient absorbtion in pigs, journal of animal science, 2011.

THANK YOU