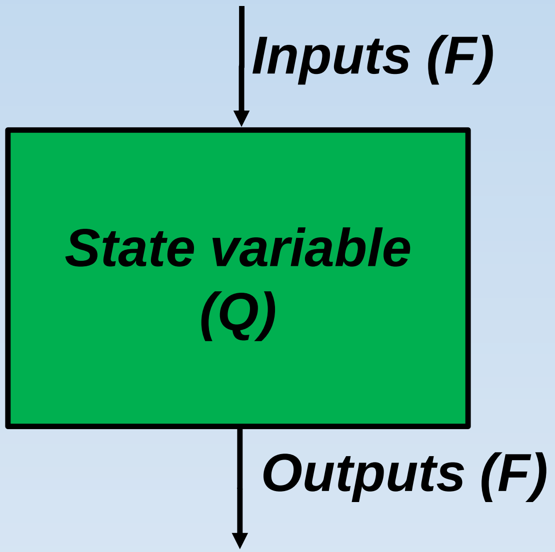
Dynamic deterministic models



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Leaning objectives

- Define what are dynamic deterministic models and explain why they are popular
- Write a model using compartmental model diagram
- Translate a model diagram into set of differential equations
- Explain different approaches for solving model equations
- Construct a model of rumen fermentation in Excel

Dynamic deterministic models

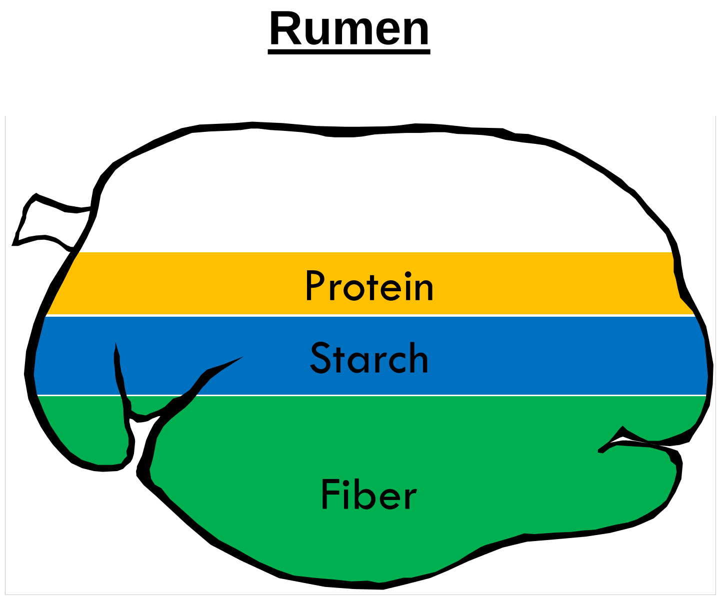
- Motivation
  - Most mechanistic models are this type
  - Used to represent almost any biological system
    - Rumen
    - Mammary gland
    - Whole animal

Dynamic deterministic models

- Principle
  - Represent biological system as set of **state variables**
  - Simulate how these variables change **over time**

Dynamic deterministic models

- Example
  - Biological system
    - Rumen
  - State variables
    - Protein
    - Starch
    - Fiber
  - Simulation
    - Change in nutrient pools over feeding cycle

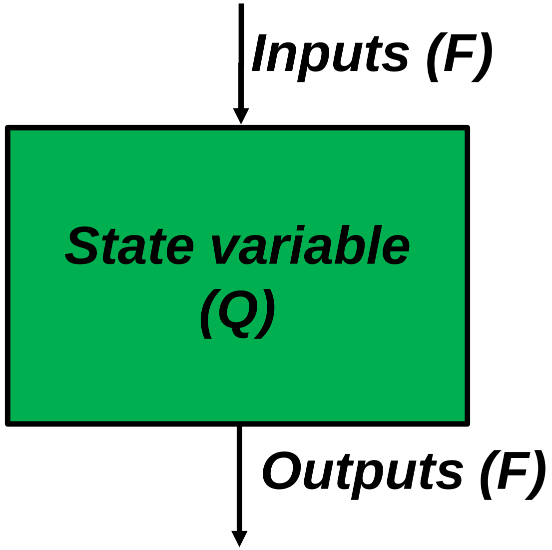


Representation

- Formally written using differential equations
- Easy to visualize with compartmental model diagrams first

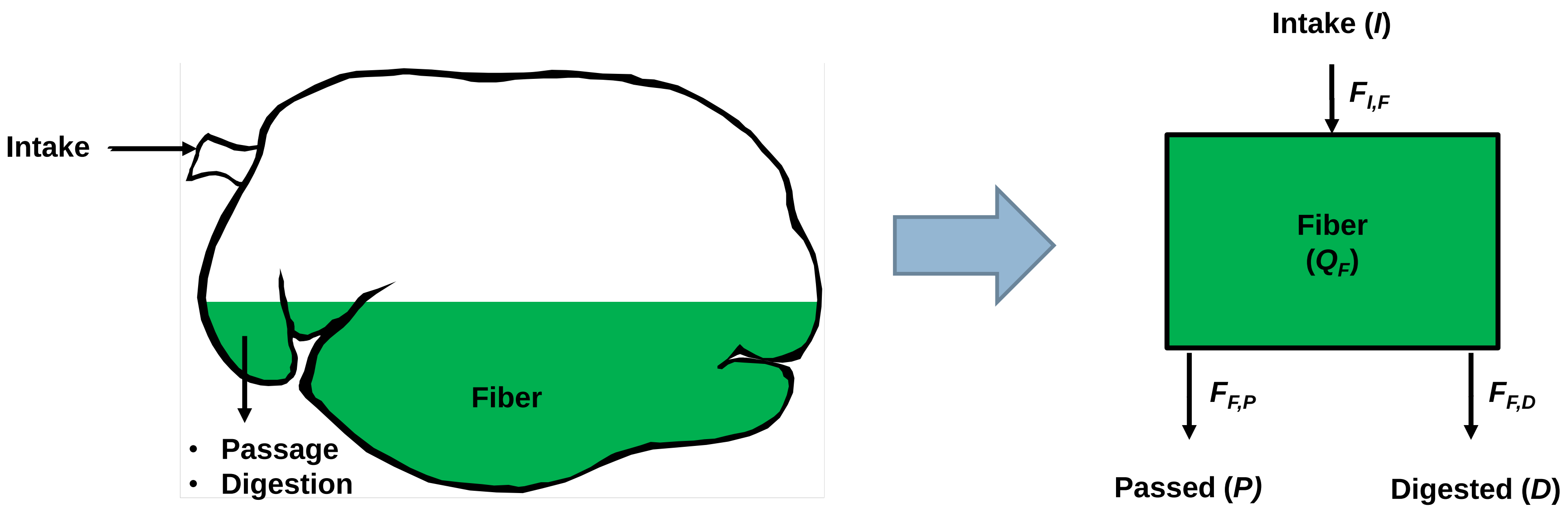
Compartmental model diagram

- Rectangle = state variable (pool)
- Arrows = inputs and outputs (fluxes)



Compartmental model diagram

- Example
  - Fiber pool in rumen

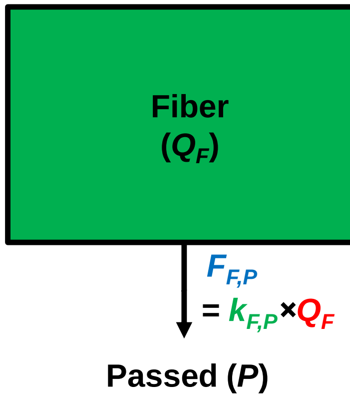


Compartmental model diagram

- Need defined inputs and outputs
  - Functions of parameters
  - Example: Passage

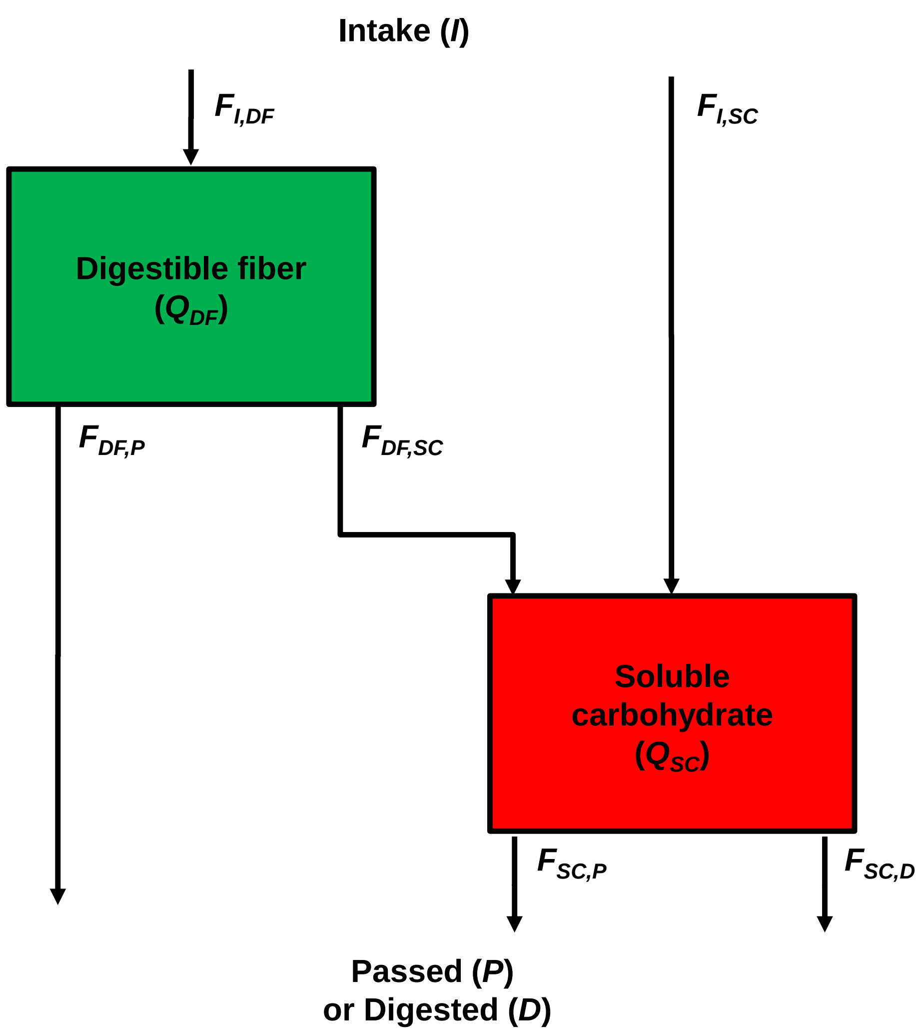
$$Passage(kg\ h^{-1}) = rate\ constant(h^{-1}) \times pool\ size\ (kg)$$

$$F_{F,P} = k_{F,P} \times Q_F$$



Compartmental model diagram

- Multiple pools connected (usually)



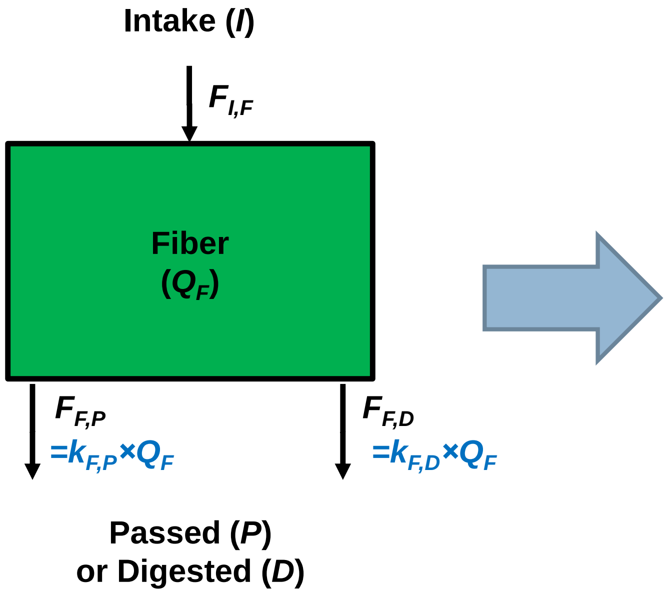
Differential equations

- Written from compartmental modeling diagram
- Define change in state variables (pools) over time

$$\frac{d(State\ variable)}{dt} = Inputs - Outputs$$

Differential equations

- Example



$$\frac{d(State\ variable)}{dt} = Inputs - Outputs$$

$$\frac{d(Q_F)}{dt} = F_{I,F} - (F_{F,P} + F_{F,D})$$

$$= F_{I,F} - (k_{F,P}+k_{F,D}) \times Q_F$$

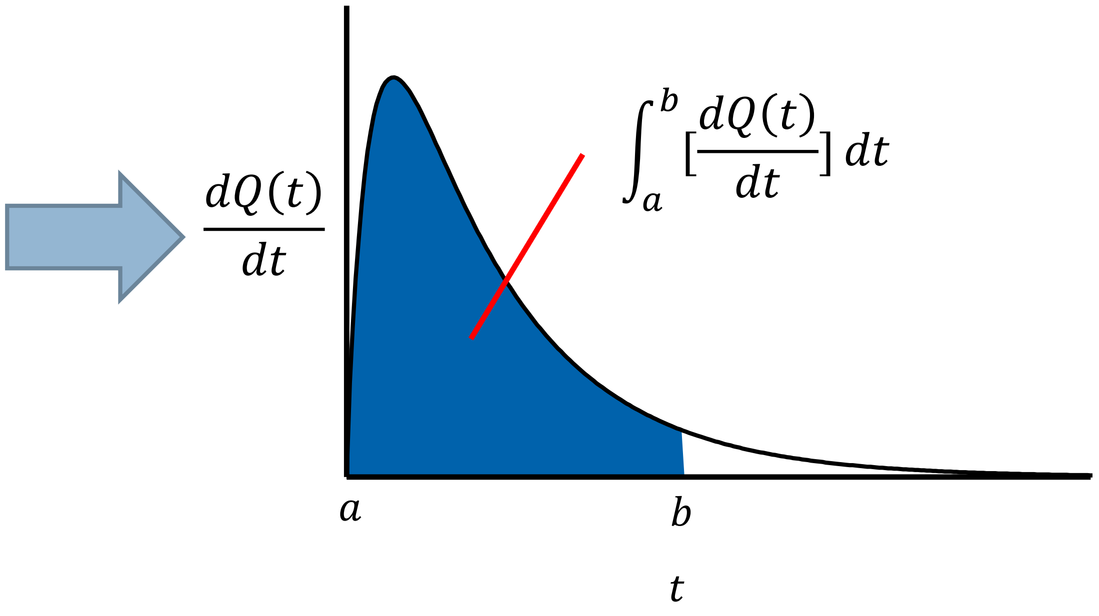
Solution

- Equations need to be solved to generate predictions
- Simple models have **analytical solutions**
- Complex models have **numerical solutions** only

Solution

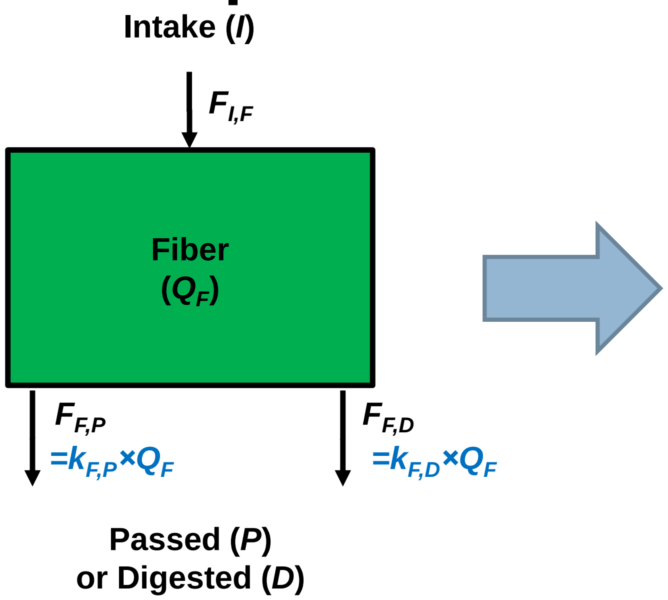
- Analytical solution
  - Integrate using rules taught in calculus courses

$$Q(t) = \int [\frac{dQ(t)}{dt}]\, dt$$



Solution

- Analytical solution
  - Example



$$Q_F(t) = \int \left[\frac{dQ_F(t)}{dt}\right] dt$$

$$= \int \left[F_{I,F} - Q_F(t) \times \left(k_{F,P} + k_{F,D}\right)\right] dt$$

$$= \frac{F_{I,F}}{k_{F,P} + k_{F,D}} + \left[Q_F(0) - \frac{F_{I,F}}{k_{F,P} + k_{F,D}}\right] \times \exp\left[-\left(k_{F,P} + k_{F,D}\right) \times t\right]$$

Make predictions by evaluating this expression at any time **t**

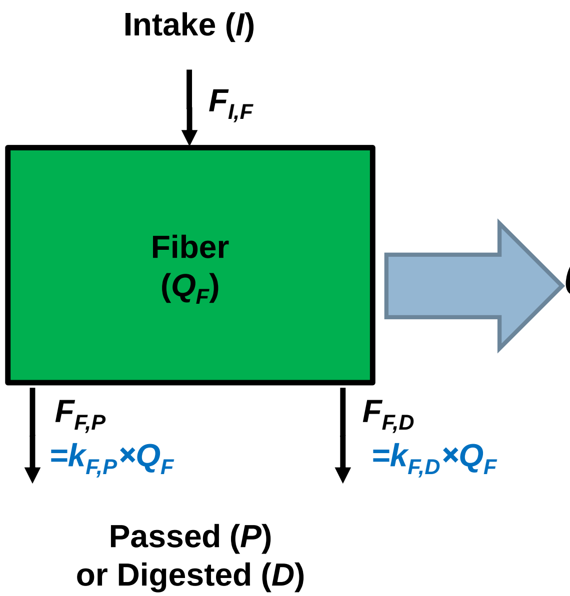
Solution

- Numerical solution
  - Integrate by calculating value numerically over short time intervals (Δt)
  - Done with **difference equations**

$$Q(t + \Delta t) \approx Q(t) + \frac{dQ(t)}{dt} \times \Delta t$$

Solution

- Numerical solution
  - Example



$$Q_F(t+\Delta t) \approx Q_F(t) + \frac{dQ_F(t)}{dt} \times \Delta t$$

$$\approx Q_F(t) + \left[F_{I,F} - k_{F,P} \times Q_F(t) - k_{F,D} \times Q_F(t)\right] \times \Delta t$$

Make predictions by evaluating this expression iteratively (over time)

Solution

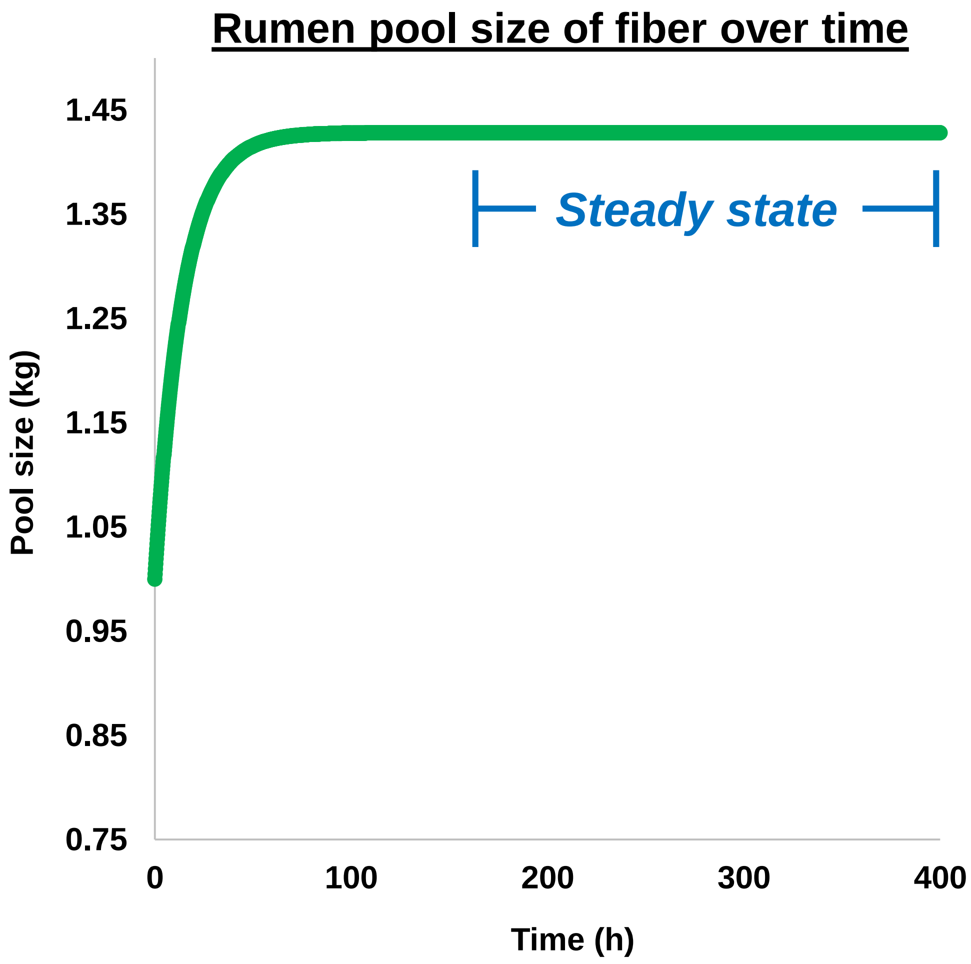
- Numerical solution
  - Methods
    - Euler
      - Method just shown
      - Easy to implement by hand in Excel or other spreadsheet
      - Relatively high error

Solution

- Numerical solution
  - Methods
    - *Euler*
    - Runge-Kutta
      - Similar to method shown, but uses difference equations with more terms
      - Need specialized software (Vensim, R, acslX) to implement
      - Relatively low error

Solution

- Steady state
  - Reached when value of state variables no longer change
  - Predictions reported for many models are at steady state



Exercises

- Demonstration
  - We will construct and use a simple (one-pool) model of rumen fermentation in Excel
- Hands-on
  - You will construct and use your own, multi-pool model

Exercises

(a) Find the steady-state solution for the pool size of indigestible fiber (Q_{IF}). Do this by coding in the difference equation in column H.

(b) Using cell D10, change $k_{DF,SC}$ from 0.05 to 0.1 h^{-1}. Which pool sizes change and why?

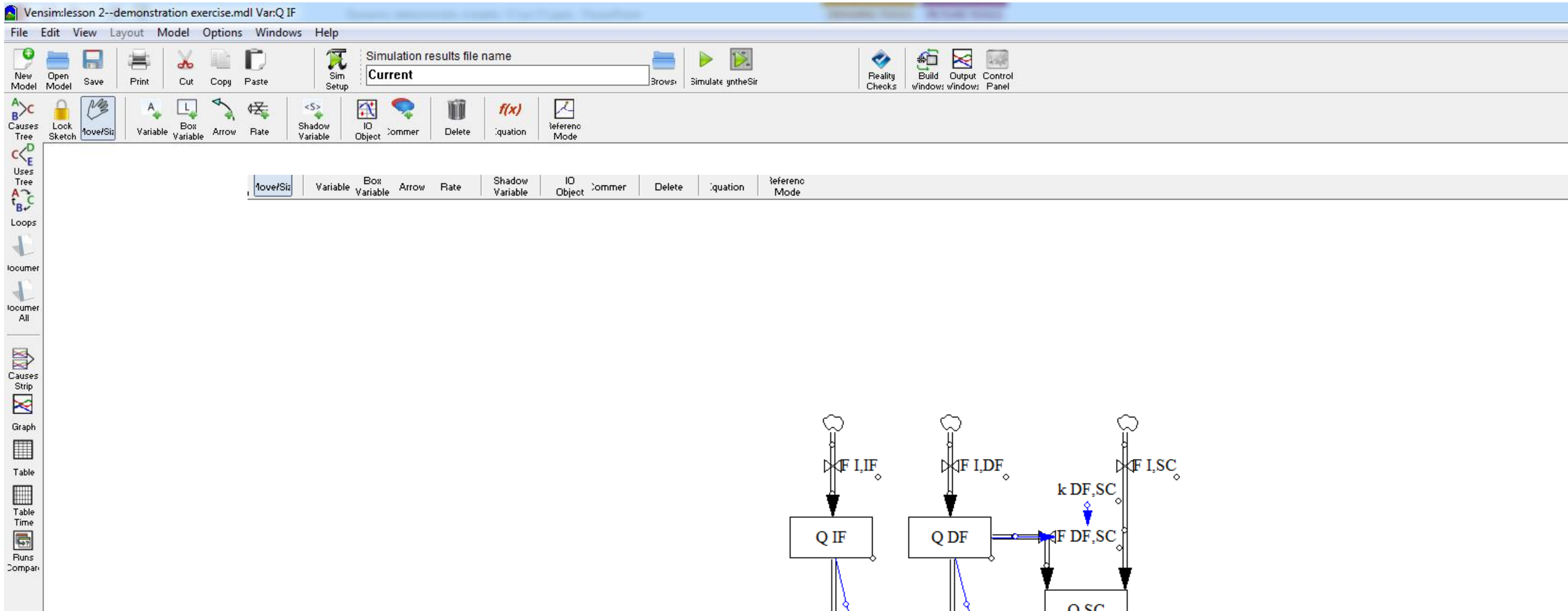
(c) Using cell D22, change the time step (Δt) to 0.01. Why do pool sizes change at steady state? Is the system really at steady state?

(d) Using cells M39 to M42, calculate $F_{SC,D}/(F_{SC,D}+F_{IF,P}+F_{DF,P}+F_{SC,P})$. What does this value represent?

Take home materials

- Model in Vensim and R
  - Files available at hackmannlab.org

Vensim



Take home messages

- Dynamic deterministic models are the classic mechanistic model
- They are formulated by drawing a compartmental diagram, then translating the diagram into differential equations
- Equations are usually solved numerically
- Simple models can be implemented in Excel, but more complex models require specialized software
- Solution requires parameter values to be defined

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Visit us at **hackmannlab.org**

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