

Slides, videos, links and more:

<https://github.com/physicell-training/ws2022>

Session 12: Intracellular with libRoadrunner



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PhysiCell Project

July 27, 2022



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What we have learned so far

- PhysiCell folder structure
- PhysiCell model domain
 - Different dts (diffusion_dt, mechanic_dt, phenotype_dt)
- Using PMB to create config file (XML)
- PhysiCell C++ functions
- And much more!

What we will learn

- Basics of Kinetic Modeling (ODE Model)
- How to integrate kinetic models to ABM
- How to control phenotype based on intracellular model
- Kinetic ODE solver (libRR) related functions
- How to save intracellular data
- How to change intracellular_dt

What we will see

- An example of how to create spheroid
- Main file additions
- How to iterate all over cells in C++
- Coloring Function

Agenda:

- First Session
 - ⑩ PhysiCell Intracellular Class
 - ⑩ Kinetic SBML
 - ⑩ PhysiCell Integration
 - Model Design
 - Results
 - Convergence Tests
 - ⑩ libRR Add-on
 - Functions
 - Phenotypic Changes
 - ⑩ Sample Model
 - Description
 - Basic Domain Creation (If we can)

PhysiCell Intracellular Class

- PhysiCell 1.9.0 = Intracellular Integrations
 - Released: 12 July 2021
- Major new features
 - Includes three intracellular modeling approaches
 - ♦ Boolean Network => PhysiBoSS
 - ♦ Kinetic Modeling (ODEs) => libroadrunner
 - ♦ Flux Balance Analysis => PhysidFBA
 - New Intracellular Object in Phenotype
 - ♦ All intracellular packages basic generic functions with same syntax
 - » Start(), Update(), get_parameter(), set_parameter(), ...
 - ♦ Some special functions specific to packages
 - » get_boolean_variable_value(PhysiBoSS) validate_SBML_species (ODE), ...

3 Sample Projects

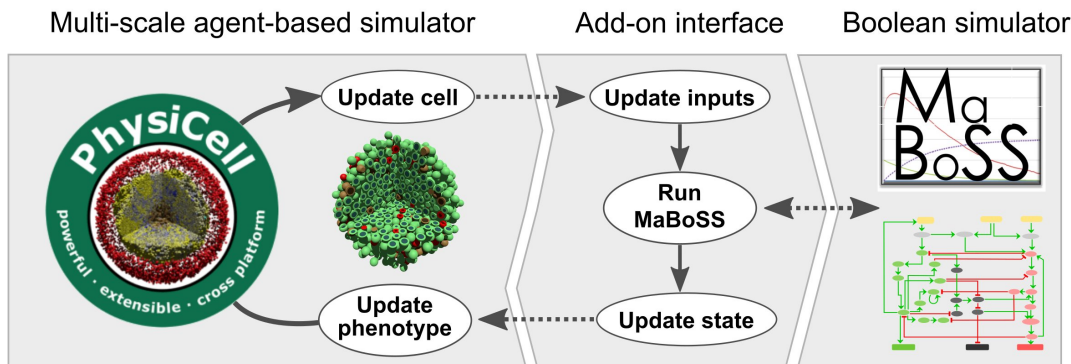
- PhysiBoSS
 - physiboss-cell-lines-sample
- Libroadrunner
 - ode-sample-project
- PhysidFBA
 - cancer-metabolism

Solvers & Installation

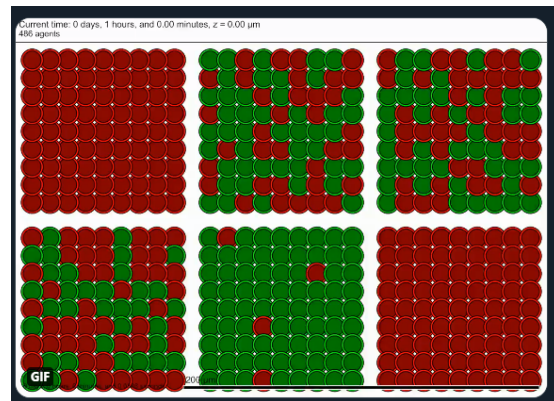
- Each add-on requires related solver
 - PhysiBoSS – MaBoSS
 - PhysidFBA – coin-clp
 - Libroadrunner – Libroadrunner (no surprise!)
- To install related solver, you need to populate sample-project, first
 - make ode-energy-sample
- Then, compile once.
 - make

PhysiBoSS

- Boolean Network
 - MaBoSS
- SysBioCurie & BSC



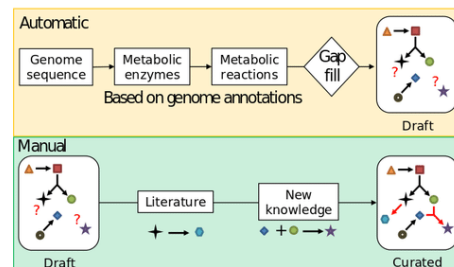
- <https://github.com/gletort/PhysiBoSS>
 - Fully integrated as “add-on” to PhysiCell
- Session 10-11:
 - Please visit [agenda](#) for slides and video



PhysidFBA

- Aims to couple ABM and FBA.
- Miguel Ponce de Leon
- Approach will be explained in future slides.
- <https://github.com/migp11/PhysiCellFBA>
 - Added alpha version as “add-on” to PhysiCell.

a) Genome-scale metabolic reconstruction



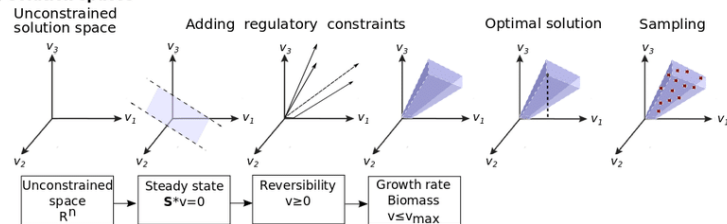
b) Flux balance analysis

Maximize/minimize an objective function
 $Z = C_1V_1 + C_2V_2 + \dots + C_5V_5$, such that:

$$\begin{matrix} \text{Reactions} \\ R_1 & R_2 & R_3 & R_4 & R_5 \end{matrix} \begin{pmatrix} -1 & 0 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 \\ 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \otimes \begin{pmatrix} V_1 \\ V_2 \\ V_3 \\ V_4 \\ V_5 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

S-matrix Flux vector
 and for every reaction i : $lb_i < v_i < ub_i$

c) Solution spaces



Heirendt et al, 2017

Libroadrunner

- Integrating intracellular kinetic models to individual agents.
- Individual phenotype changes according to molecular simulations
 - Intracellular values (Molecular Concentrations, Signal Transductions, i.e.)
 - ♦ Intracellular oxygen deficiency in cell leads to change necrosis rate.
 - ♦ Intracellular amino acids levels define the cellular growth / cycle rate.
- Opens new opportunities for PhysiCell syntax
 - Users can utilize SBML to model phenotypic behaviors.
 - Since molecular values can edit phenotypic parameters in SBML, PhysiCell interface is getting changed.
- LibRR is developed by
 - Herbert Sauro and Andy Somogyi
 - C++ API

SBML

- Systems Biology Mark-up Language
- Reaction – Stoichiometry
- Kinetic – Pseudo Steady State
 - Kinetic – Ordinary Differential Equations
 - Pseudo Steady State – Optimization (Flux Balance Analysis)
- Hard to read for Human (xml file)
- Parsed according to some rules.

```
[...]
<species metaid="heme"
  id="heme"
  compartment="Comp01"
  initialConcentration="0">
  <annotation>
    <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
      xmlns:bqbiol="http://biomodels.net/biology-qualifiers/">
      <rdf:Description rdf:about="#heme">
        <bqbiol:hasPart>
          <rdf:Bag>
            <rdf:li rdf:resource="urn:miriam:uniprot:P69905" />
            <rdf:li rdf:resource="urn:miriam:uniprot:P68871" />
            <rdf:li rdf:resource="urn:miriam:obo.chebi:CHEBI%3A17627" />
          </rdf:Bag>
        </bqbiol:hasPart>
      </rdf:Description>
    </rdf:RDF>
  </annotation>
</species>
[...]
```

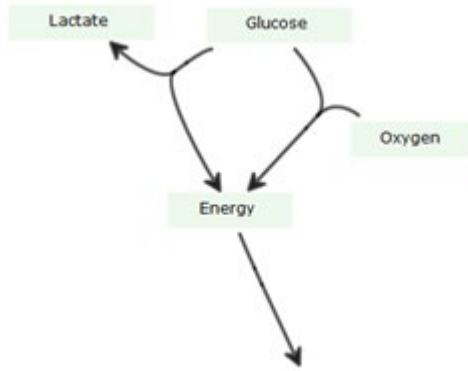
SBML

- Compartments
 - Volumetric Entities
- Species
 - Chemicals
- Reactions
 - Stoichiometric Relations
 - Boundaries (Lower and Upper) (FBA)
- Global Quantities
 - Parameters
 - Constants

```
▼ COPASI
  ▼ Model
    ▼ Biochemical
      ▼ Compartments [1]
        Intracellular
      ▼ Species [4]
        Energy
        Glucose
        Lactate
        Oxygen
      ▼ Reactions [3]
        Aerobic
        Anaerobic
        Energy_Usage
      ▼ Global Quantities [3]
        k_aer
        k_ane
        k_usage
```

#	Name	Reaction	Rate Law	Flux [mmol/min]	Noise Expression
1	Aerobic	Glucose + 6 * Oxygen -> 38 * Energy	Mass action (irreversible)	nan	
2	Anaerobic	Glucose -> 2 * Energy + Lactate	Mass action (irreversible)	nan	
3	Energy_Usage	Energy ->	Mass action (irreversible)	nan	
	New Reaction				

Kinetic Modeling



#	Name	Reaction
1	Aerobic	Glucose + 6 * Oxygen -> 38 * Energy
2	Anaerobic	Glucose -> 2 * Energy + Lactate
3	Energy_Usage	Energy ->
	New Reaction	

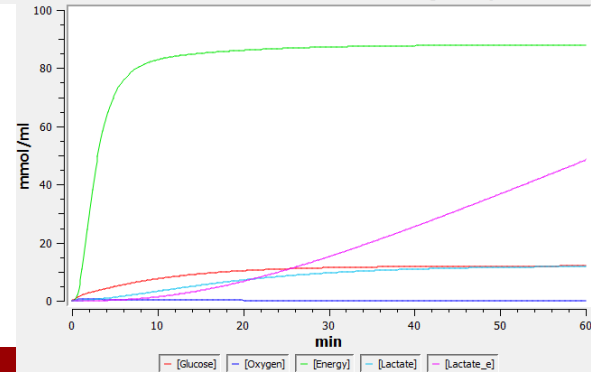
$$\frac{d([Glucose] \cdot V_{Intracellular})}{dt} = -V_{Intracellular} \cdot (k_{aer} \cdot [Glucose] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen]) - V_{Intracellular} \cdot (k_{ane} \cdot [Glucose])$$

$$\frac{d([Oxygen] \cdot V_{Intracellular})}{dt} = -6 \cdot V_{Intracellular} \cdot (k_{aer} \cdot [Glucose] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen])$$

$$\frac{d([Energy] \cdot V_{Intracellular})}{dt} = +38 \cdot V_{Intracellular} \cdot (k_{aer} \cdot [Glucose] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen] \cdot [Oxygen]) + 2 \cdot V_{Intracellular} \cdot (k_{ane} \cdot [Glucose]) - V_{Intracellular} \cdot (k_{usage} \cdot [Energy])$$

$$\frac{d([Lactate] \cdot V_{Intracellular})}{dt} = +V_{Intracellular} \cdot (k_{ane} \cdot [Glucose])$$

Concentrations, Volumes, and Global Quantity Values

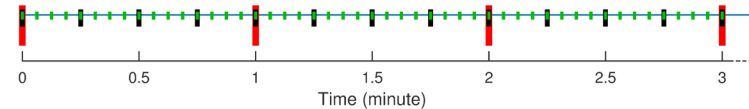


SBML

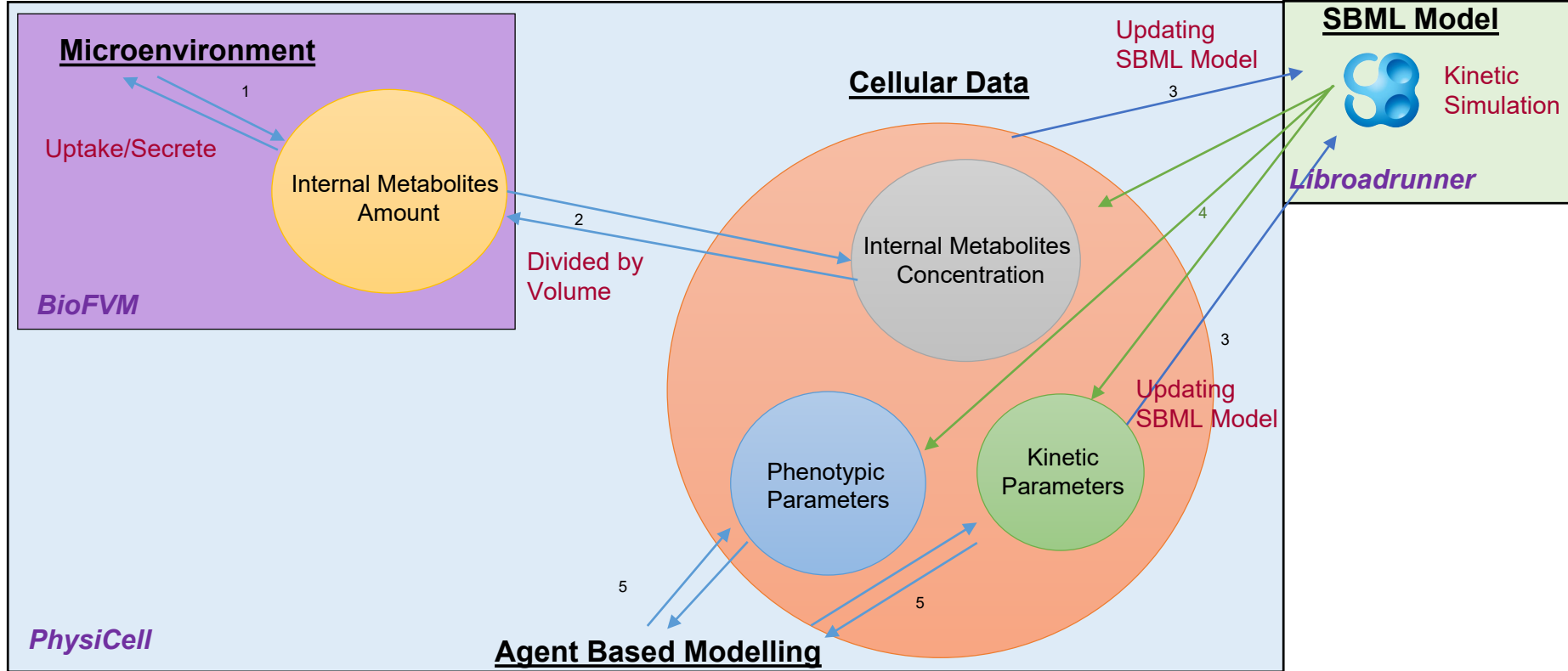
- General SBMLs have more than one compartment
 - Extracellular
 - Intracellular
 - Mitochondria (Sometimes)
 - Nucleus (?)
- And have two or more species for one substrate
 - Glucose[e] => extracellular
 - Glucose[i] => intracellular
- Transfer reaction between compartments
 - Glucose[e] = Glucose[i]

Assumptions

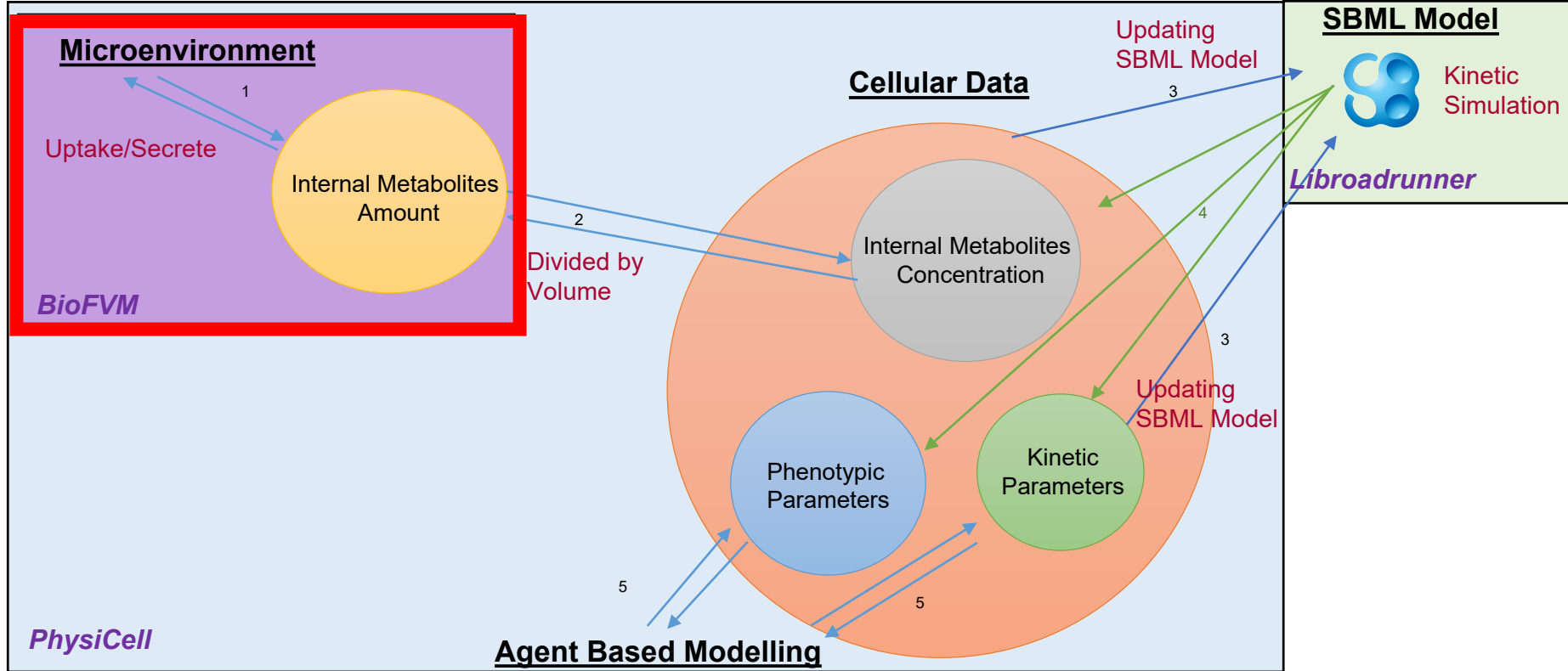
- **But ...**
- PhysiCell has transfer reactions through
 - BioFVM
- So, we can support specific type of SBMLs
 - Only Intracellular (might have more than one compartment – Mitochondria, Nucleus)
- Well-Structured SBMLs
 - **Not all SBMLs are supported!!!**
 - ♦ No External Compartment and Transfer Reactions in SBML!
 - ♦ Mapping is needed between SBML & PhysiCell
 - Works on each diffusion_dt (0.01 min)
 - ♦ (as default for best convergence/can be changed)



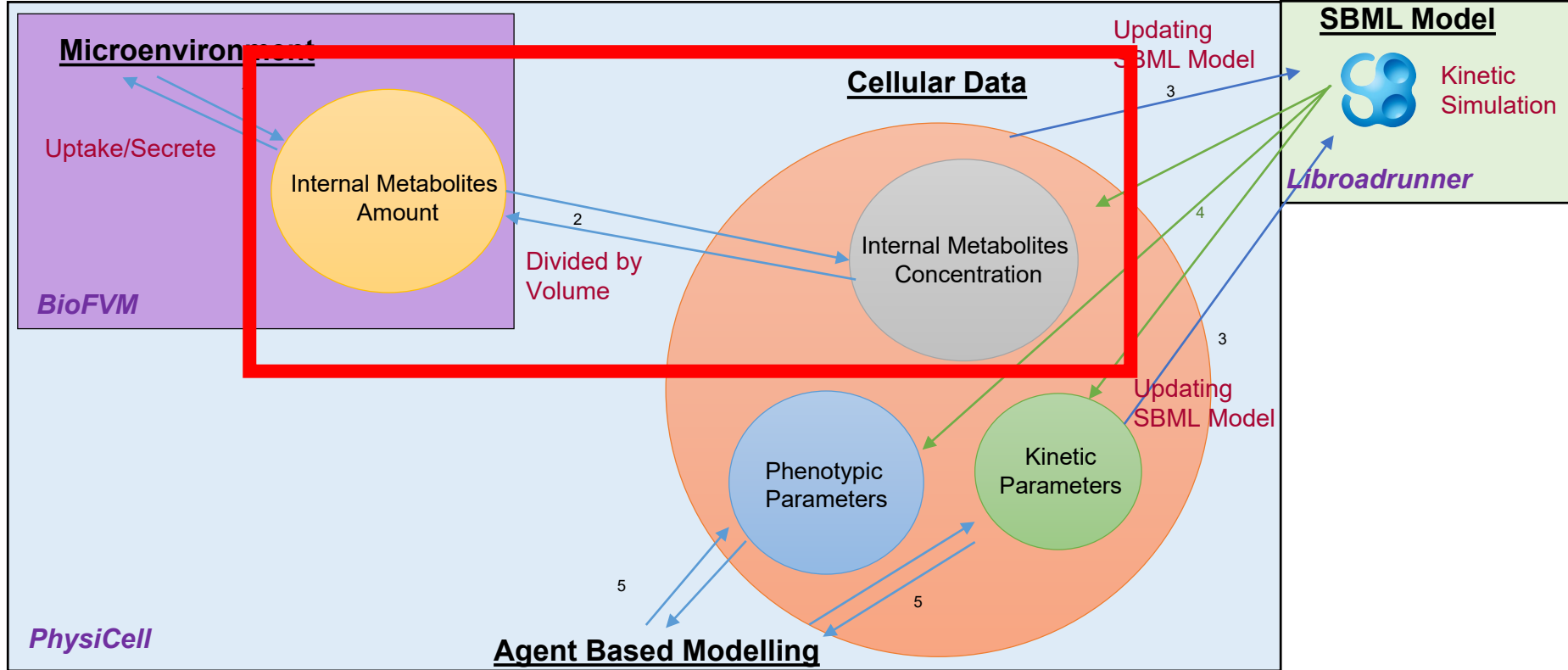
Integration Design



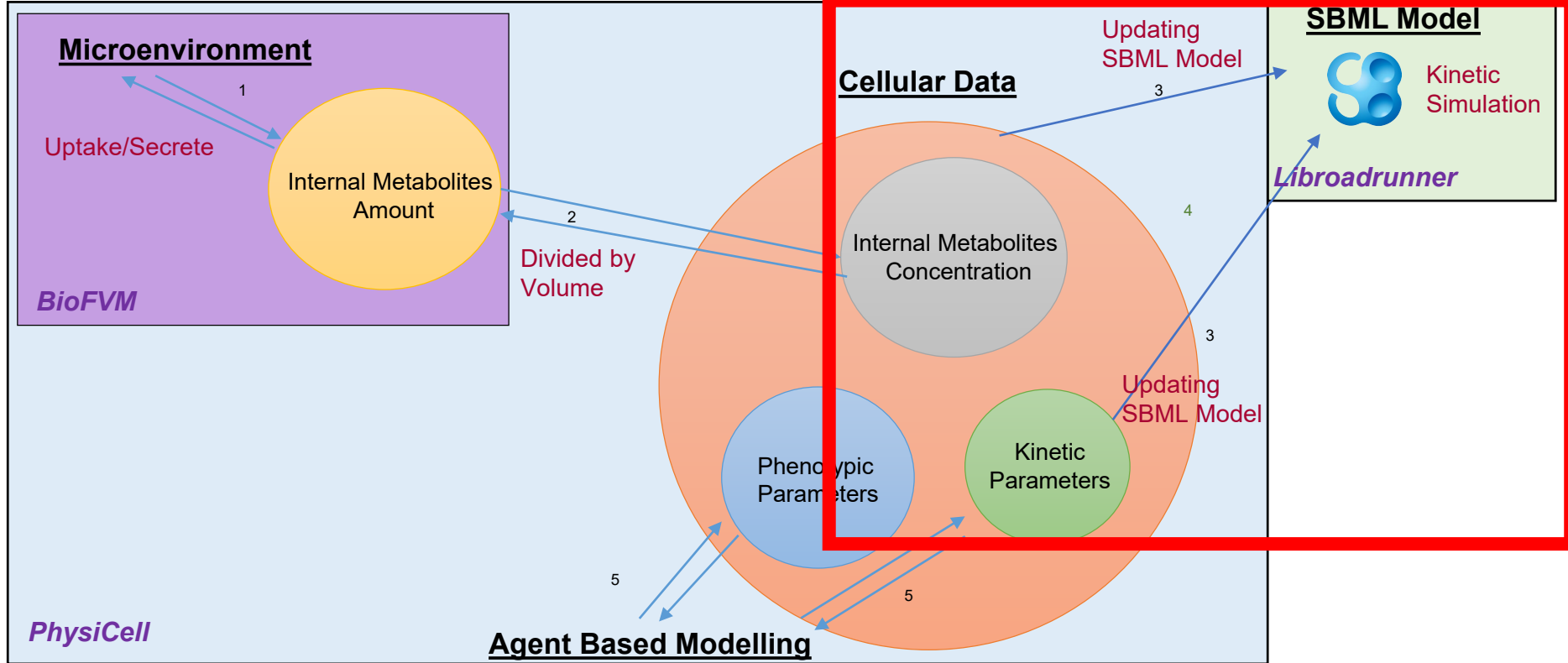
Integration Design



Integration Design



Integration Design



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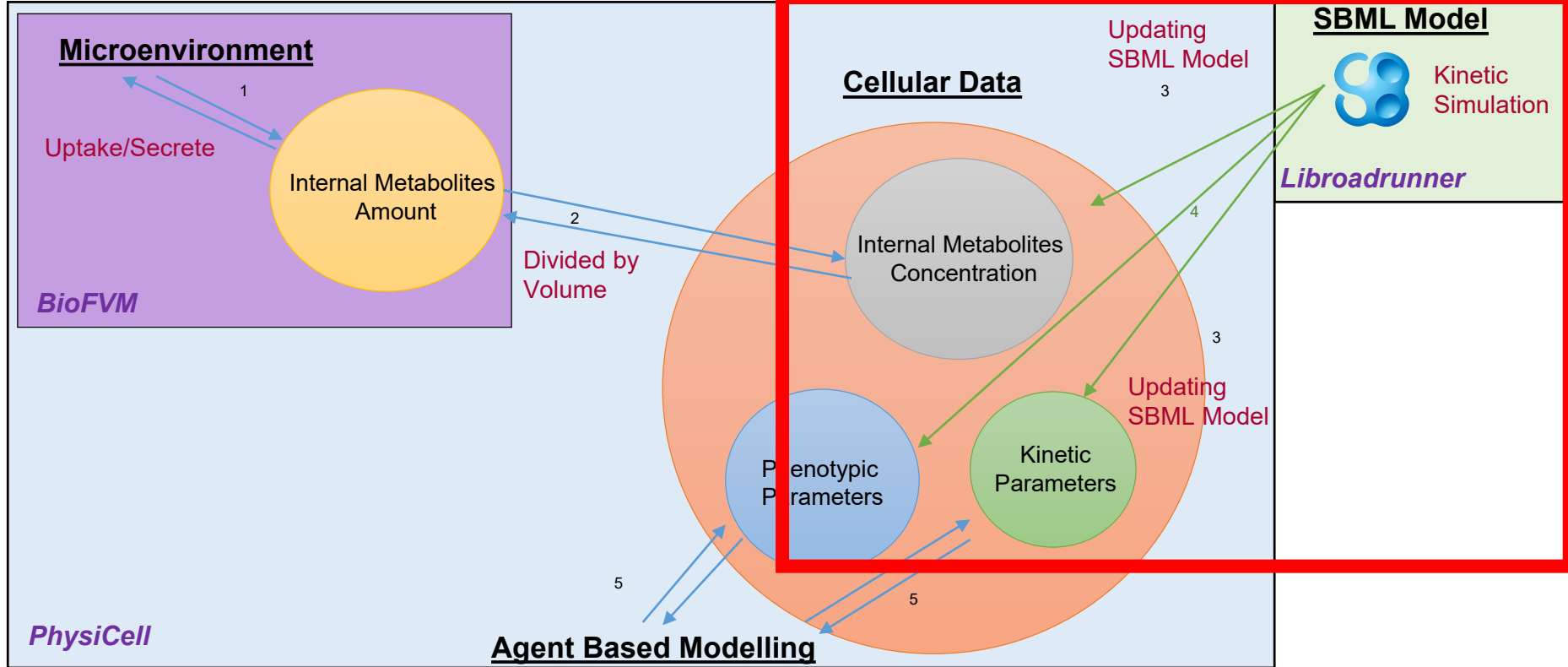
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Integration Design



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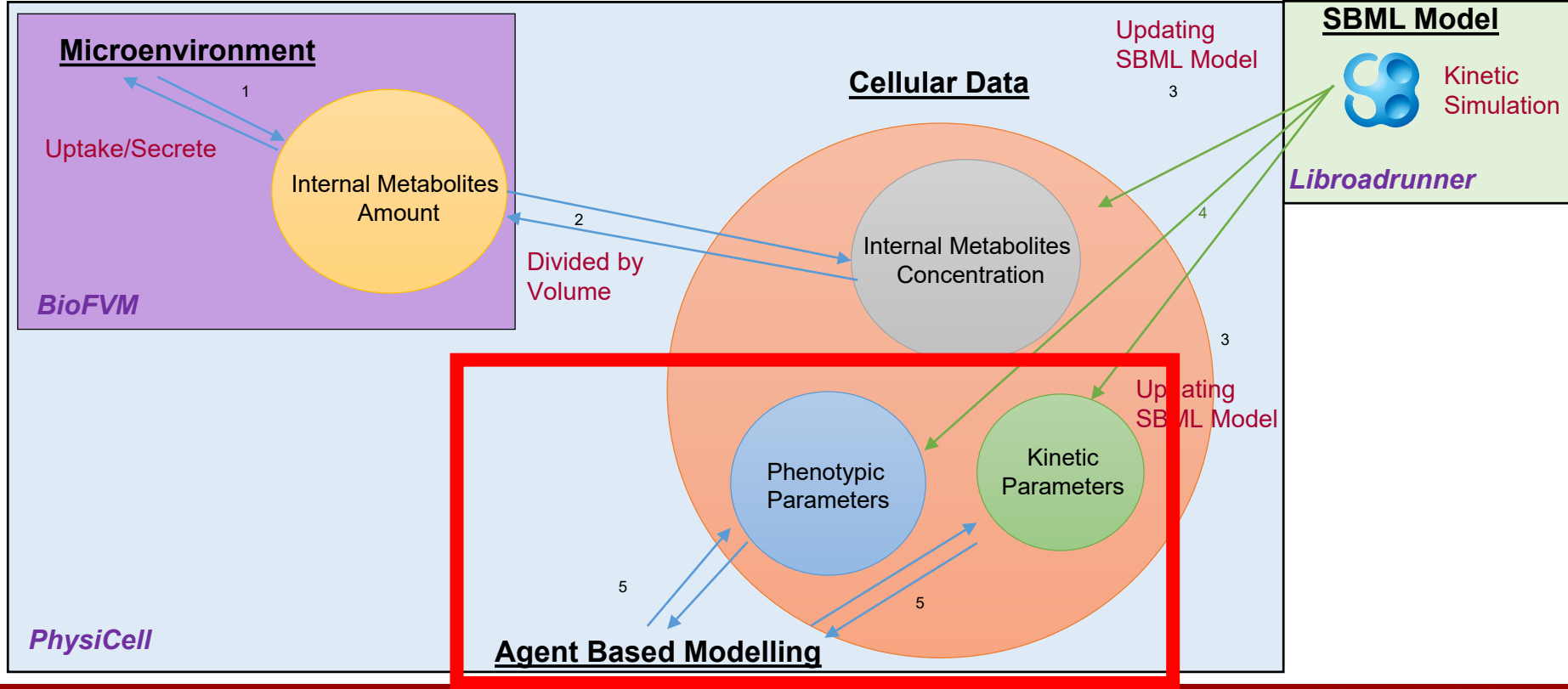
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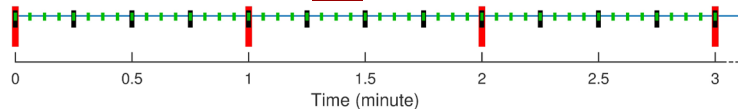
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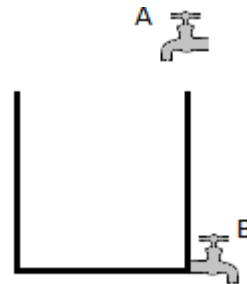
Integration Design



How about intracellular_dt



- Default 0.01 min but...
- We can change intracellular_dt
- As we are working with rate, you don't have to change the parameters
- Time units will match
- We can change intracellular_dt but updating less can produce some convergence errors.



How it looks

- Config File

```
<cell_definitions>
  <cell_definition name="default" ID="0">
    <phenotype>
      <cycle code="5" name="live">
        <!-- using higher than normal significant digits to match divisions in default code -->
        <transition_rates units="1/min">
          <rate start_index="0" end_index="0" fixed_duration="false">0.0</rate>
        </transition_rates>
      </cycle>
      <death>
      </death>
      <volume>
      </volume>
      <motility>
        <speed units="micron/min">0.0</speed>
        <persistence_time units="min">0.1</persistence_time>
        <migration_bias units="dimensionless">.9</migration_bias>
        <options>
          <enabled>true</enabled>
          <use_2D>true</use_2D>
          <chemotaxis>
            <enabled>false</enabled>
            <substrate>oxygen</substrate>
            <direction>1</direction>
          </chemotaxis>
        </options>
      </motility>
      <secretion>
        <intracellular type="roadrunner">
          <sbml_filename>./config/Toy_oxy_mms_tr_01.xml</sbml_filename>
          <map PC_substrate="oxygen" sbml_species="Oxy"></map>
          <map PC_custom_data="PC_Test_CD" sbml_species="death_rate"></map>
          <map PC_phenotype="ctr00" sbml_species="transition_rate_0_1"></map>
          <map PC_phenotype="mms" sbml_species="migration_speed"></map>
          <map PC_phenotype="da" sbml_species="death_rate"></map>
          <map PC_phenotype="ssr1" sbml_species="secretion_rate_Lactate"></map>
          <map PC_phenotype="test" sbml_species="test"></map>
        </intracellular>
      </secretion>
    </phenotype>
  </cell_definition>
</cell_definitions>
```


SBML-Phenotypic Parameters

PhysiCell Phenotype Parameter	First letter	phenotype_token	example
Phase Transition Rate	c	ctr_**	ctr_0_1
Death Rate	d	da,dn	da,dn
Persistence Time	m	mpt	mpt
Migration Speed	m	mms	mms
Migration Bias	m	mmb	mmb
Uptake rate	s	sur_*	sur_oxygen
Secretion rate	s	ssr_*	ssr_glucose
Saturation density	s	ssd_*	ssd_oxygen
Export rate	s	ser_*	ser_lactate
Target solid cytoplasmic	v	vtsc	vtsc
Target solid nuclear	v	vtsn	vtsn
Target fluid fraction	v	vff	vff



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Some Results



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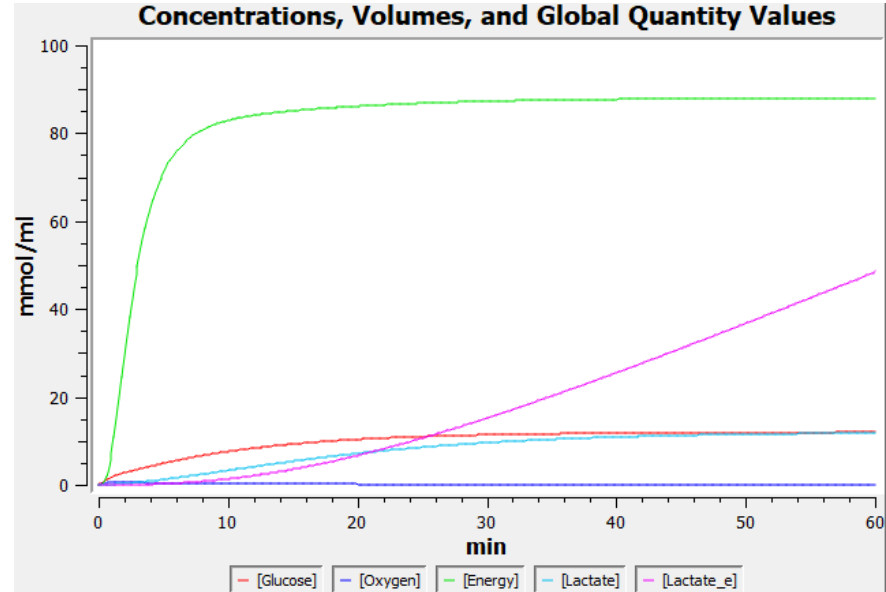
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Model 0 - SBML Model

- 4 Species
 - Oxygen
 - Glucose
 - Lactate
 - Energy
- 3 Internal Reactions
 - ♦ Aerobic reaction
 - » $\text{Glucose} + \text{Oxygen} \rightarrow \text{Energy}$
 - ♦ Anaerobic reaction
 - » $\text{Glucose} \rightarrow \text{Energy} + \text{Lactate}$
 - ♦ Energy Usage
 - » $\text{Energy} \rightarrow$



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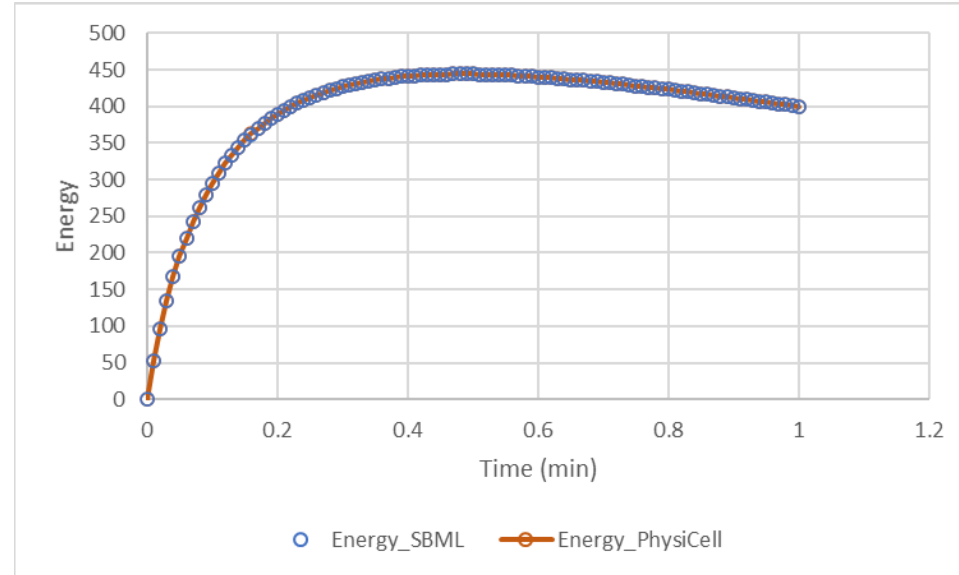
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Model 0

- Very Simple SBML toy model
- Both simulated in PhysiCell and Copasi
- No Transfer Reaction in SBML
- No Uptake Rate
- Only solving SBML



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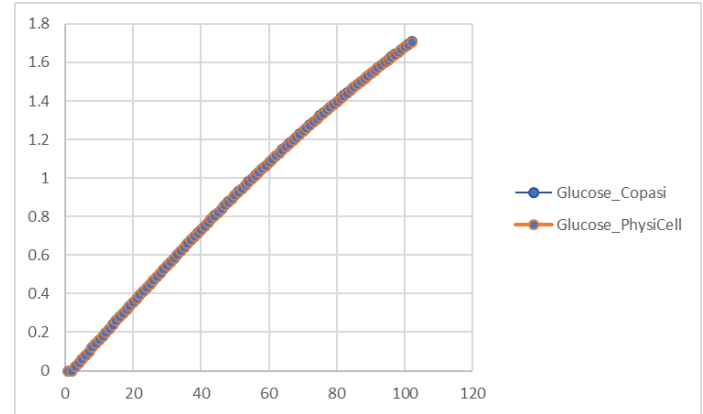
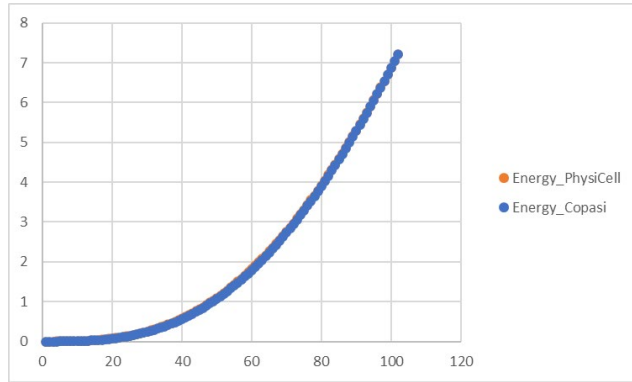
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Model 1

- Uptake glucose, oxygen
- Produces Energy internally.



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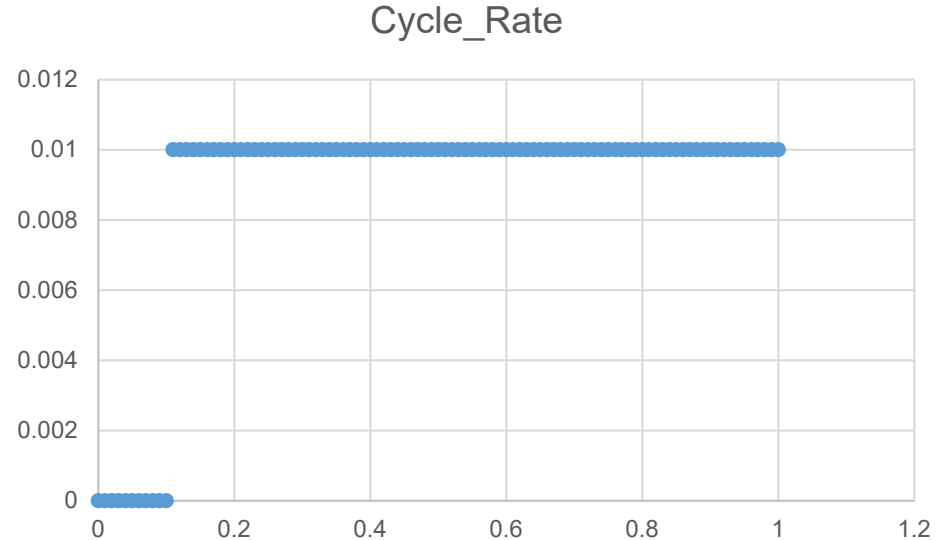
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SBML Events

Cycle Rate

- If Energy level is smaller than 50 a.u.
 - Equals to zero 1/min
- If Energy level is greater than 50 a.u.
 - Equals to 0.01 1/min



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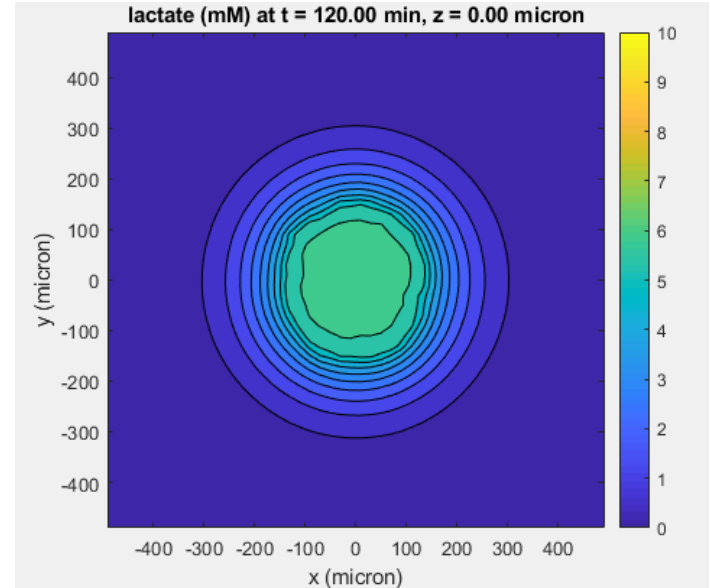
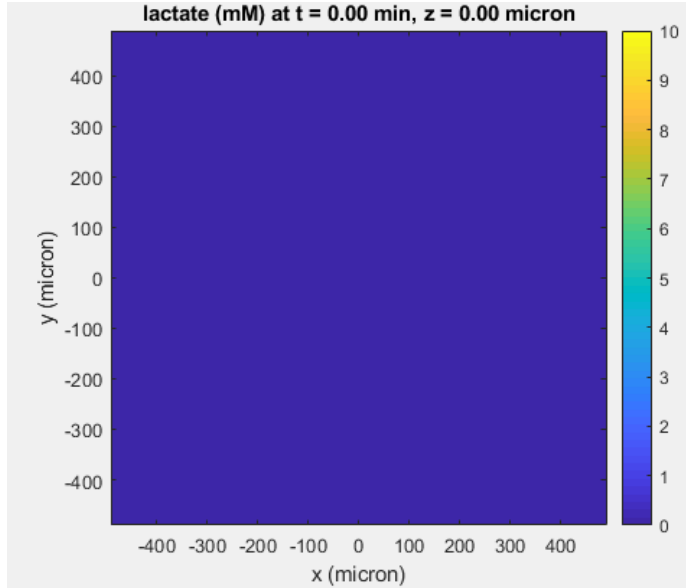
PhysiCell.org

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Model 2

- Phenotypic changes according to SBML species
- Organoid (2D) seeding.
- Lactate Secretion Rate increases
 - Lactate Concentration
- If oxygen level is less than threshold
 - Cells increase their migration speed
- If Energy level is less than threshold
 - Cells go apoptosis

Lactate Secretion



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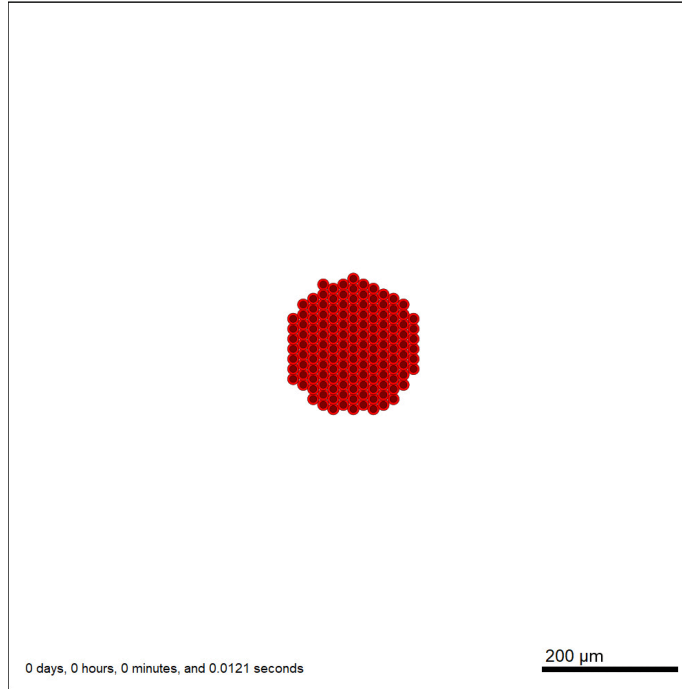
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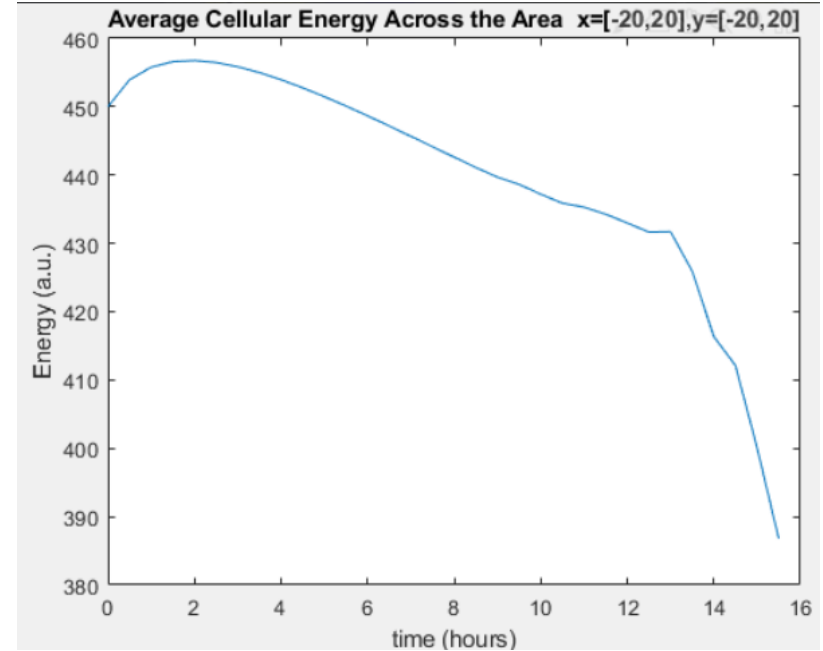
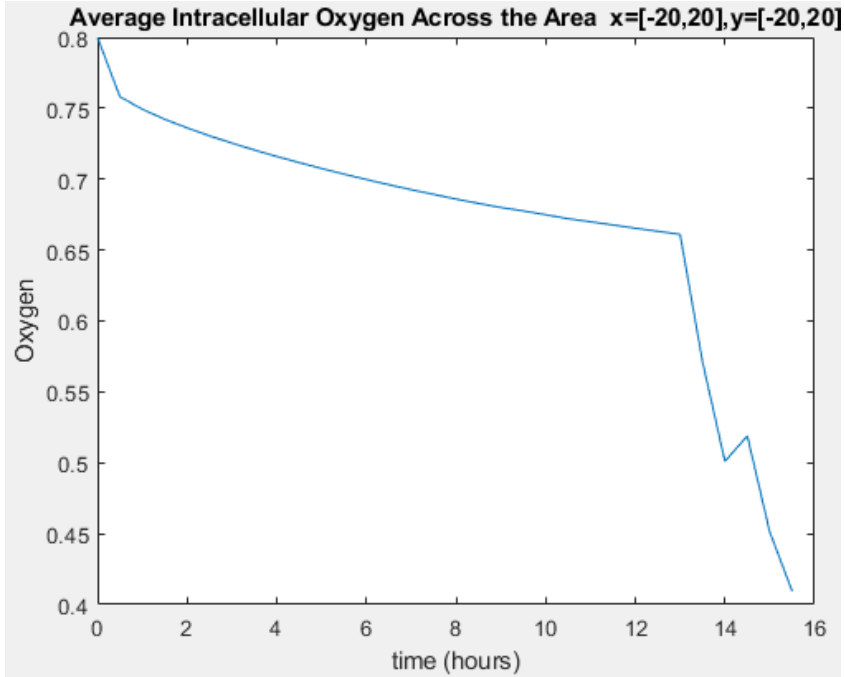
Current time: 0 days, 0 hours, and 0.00 minutes, $z = 0.00 \mu\text{m}$
144 agents



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Intracellular



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Libroadrunner Addon

- Same format for intracellular addons. (PhysiFBA, PhysiBoSS)
- Libroadrunner
 - **start()** = start intracellular in cell (it should be used after seeding and is called after proliferation)
 - **Initialize_SBML()** = to read SBML (users will not use)
 - **get_values()** = to get value from SBML
 - **set_values()** = to set value in SBML
 - **update()** = to simulate SBML
 - **get_state()** = to get the name of SBML
 - **update_phenotypic_parameters()** = to update phenotype according to given tokens
 - **validate_tokens()** = to validate given token
 - **validate_species()** = to validate SBML species



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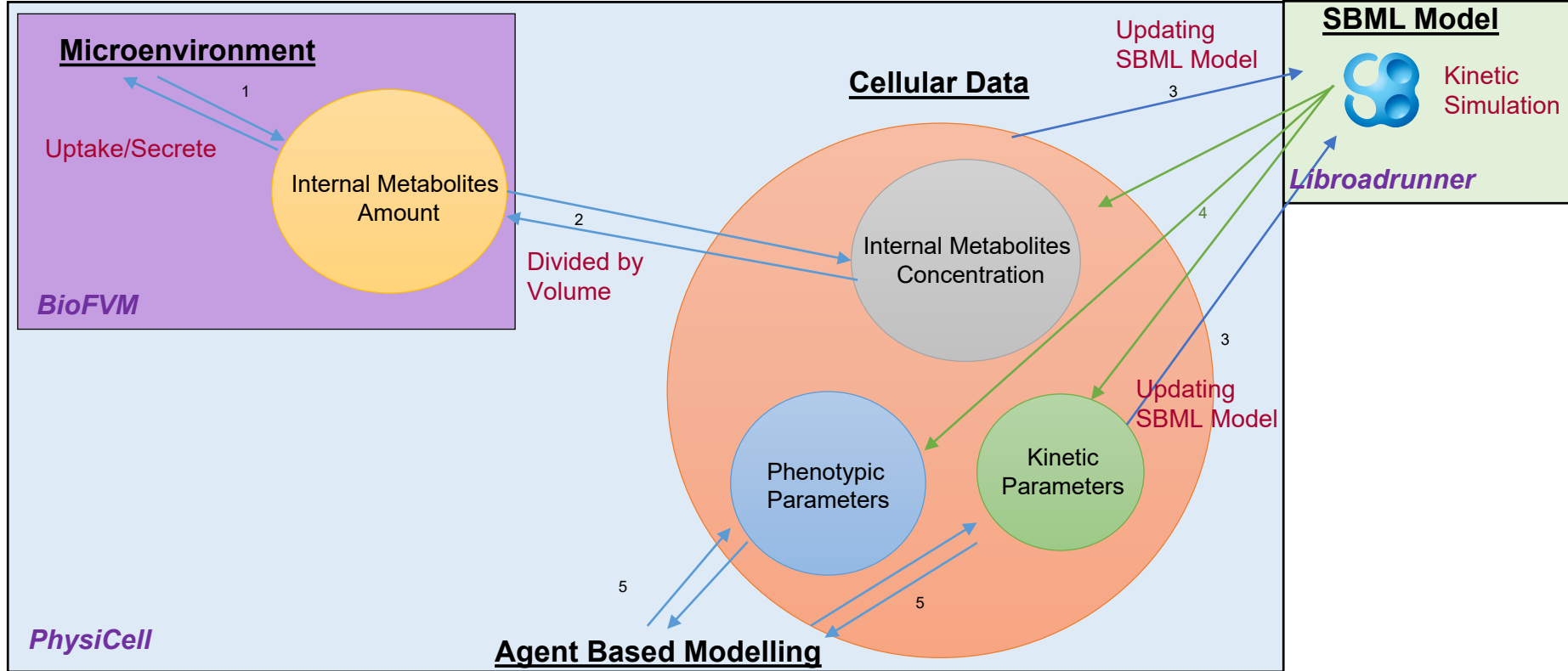
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Integration Design



SBML-Phenotypic Parameters

PhysiCell Phenotype Parameter	First letter	phenotype_token	example
Phase Transition Rate	c	ctr_**	ctr_0_1
Death Rate	d	da,dn	da,dn
Persistence Time	m	mpt	mpt
Migration Speed	m	mms	mms
Migration Bias	m	mmb	mmb
Uptake rate	s	sur_*	sur_oxygen
Secretion rate	s	ssr_*	ssr_glucose
Saturation density	s	ssd_*	ssd_oxygen
Export rate	s	ser_*	ser_lactate
Target solid cytoplasmic	v	vtsc	vtsc
Target solid nuclear	v	vtsn	vtsn
Target fluid fraction	v	vff	vff



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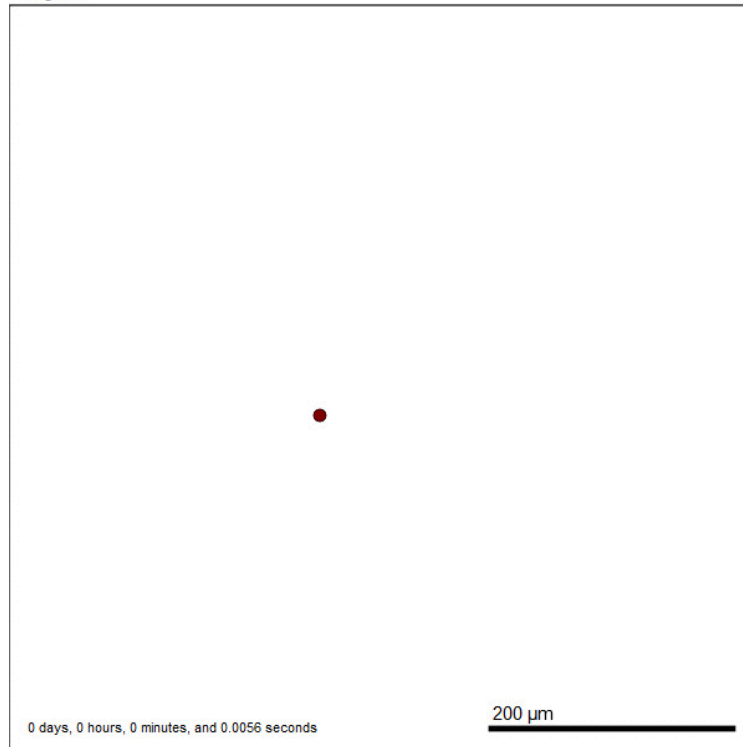
Migration Speed

Cell Definition

```
<motility>
  <speed units="micron/min">0.0</speed>
  <persistence_time units="min">0.1</persistence_time>
  <migration_bias units="dimensionless">.9</migration_bias>
  <options>
    . . . . .
```

```
<intracellular type="roadrunner">
  <sbml_filename>./config/Toy_oxy_mms_tr_01.xml</sbml_filename>
  <map PC_substrate="oxygen" sbml_species="Oxy"></map>
  <map PC_custom_data="PC_Test_CD" sbml_species="death_rate"></map>
  <map PC_phenotype="mms" sbml_species="migration_speed"></map>
</intracellular>
. . .
```

Current time: 0 days, 0 hours, and 0.00 minutes, z = 0.00 μm
1 agents

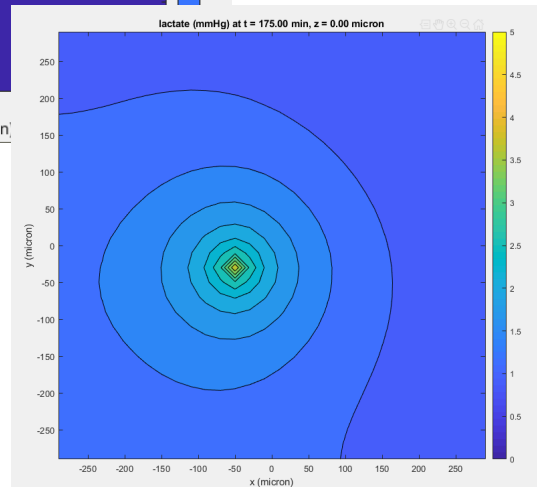
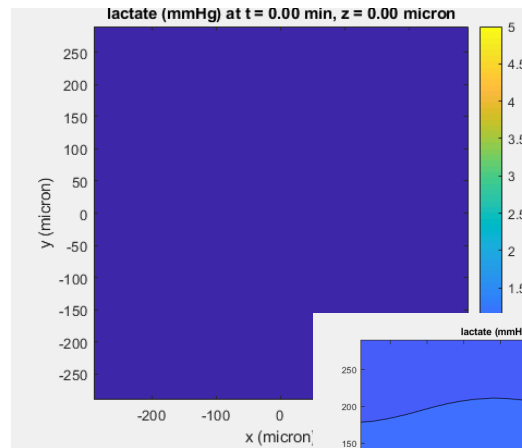


Lactate Distribution

Cell Definition

```
<secretion_rate units="1/min">0</secretion_rate>  
<secretion_target units="substrate density">10</secretion_target>  
<uptake_rate units="1/min">0.0</uptake_rate>  
<net_export_rate units="total substrate/min">0</net_export_rate>  
</substrate>
```

```
<intracellular type="roadrunner">  
  <sbml_filename>./config/Toy_oxy_mms_tr_01.xml</sbml_filename>  
  <map PC substrate="oxygen" sbml species="Oxy"></map>  
  <map PC phenotype="ssr1" sbml species="secretion_rate_Lactate"></map>  
</intracellular>
```



Wrong Tokens

```
<intracellular type="roadrunner">
  <sbml_filename>./config/Toy_oxy_mms_tr_01.xml</sbml_filename>
  <map PC_substrate="oxygen" sbml_species="Oxy"></map >
  <map PC_custom_data="PC_Test_CD" sbml_species="death_rate"></map>
  <map PC_phenotype="ctr00" sbml_species="transition_rate_0_1"></map>
  <map PC_phenotype="ssr1" sbml_species="secretion_rate_Lactate"></map>
  <map PC_phenotype="mtr1" sbml_species="test"></map>
  <map PC_phenotype="WRONG_TOKEN" sbml_species="test"></map>
</intracellular>
```

ERROR: There is no specified token parameters in the name of "mtr1" at motility parameters. Please take a look token specifications.

PS C:\Users\Furkan\Documents\GitHub\PhysiCell-SBML-trials\PhysiCell_intracellular_Phenotype>

ERROR: There is no specified token parameters in the name of "WRONG_TOKEN" at phenotypic parameters. Please take a look token specifications.



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Code walk

- Let's do code walk together...

PhysidFBA



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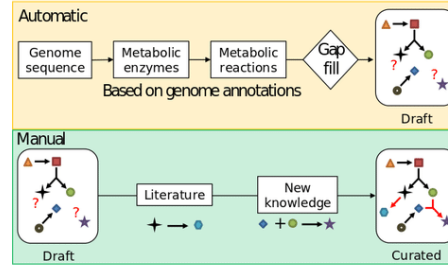
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Flux Balance Analysis

a) Genome-scale metabolic reconstruction



b) Flux balance analysis

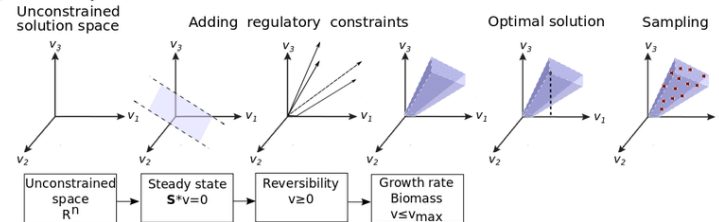
Maximize/minimize an objective function
 $Z = c_1 v_1 + c_2 v_2 + \dots + c_n v_n$, such that:

$$\begin{array}{c} \text{Metabolites} \end{array} \begin{array}{c} \text{Reactions} \\ R_1 \quad R_2 \quad R_3 \quad R_4 \quad R_5 \end{array} \begin{pmatrix} -1 & 0 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 1 & 0 & 0 & -1 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \begin{array}{c} \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{pmatrix} \\ \cong \\ \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \end{array}$$

S-matrix Flux vector

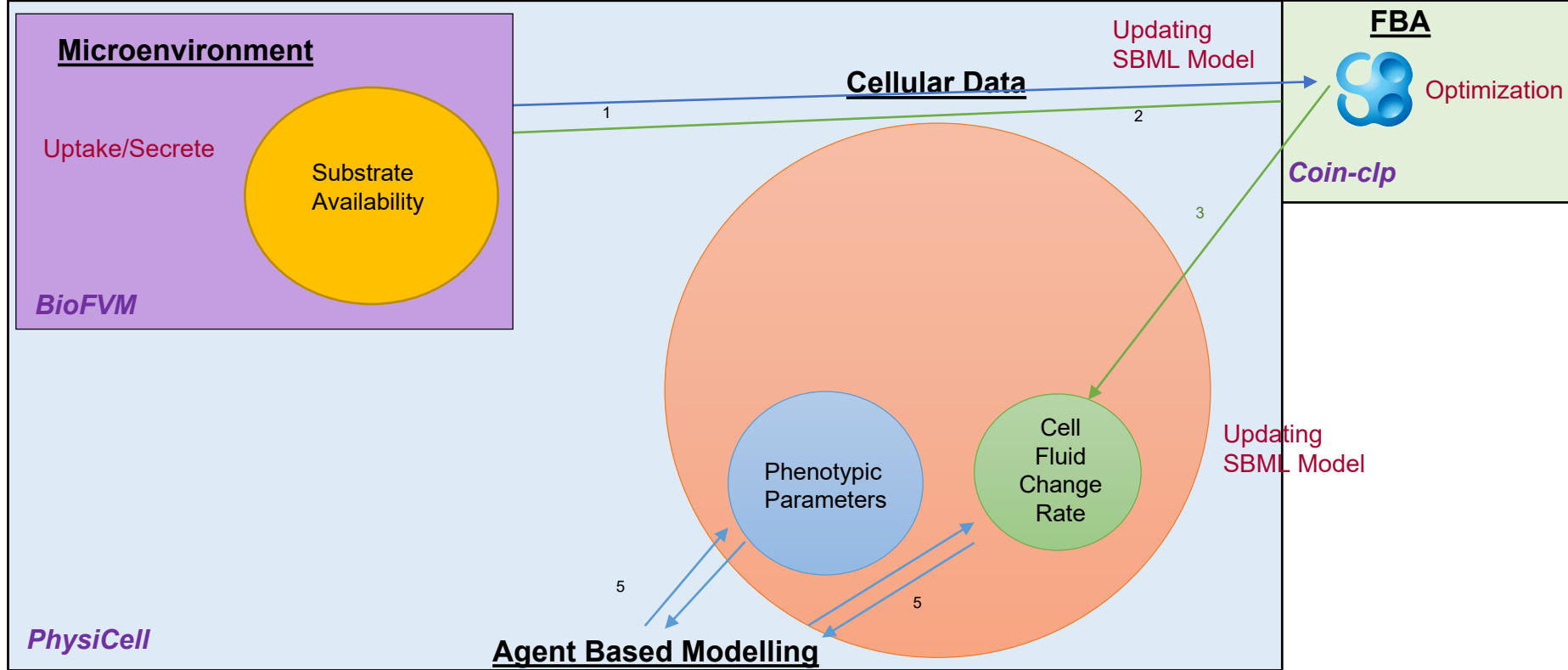
and for every reaction i : $lb_i < v_i < ub_i$

c) Solution spaces



Heirendt et al, 2017

Integration Design



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LibRoadRunner Interactive Demo



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Model

- Three Substrates
 - Oxygen, Glucose, Lactate
 - Energy is created with two reactions
 - ♦ Glucose + Oxygen \rightarrow 38 * Energy (Aerobic)
 - ♦ Glucose \rightarrow 4 * Energy + Lactate (Anaerobic)
 - Energy consumes
 - ♦ Energy \rightarrow (Energy_Usage)
- Phenotypic Tokens
 - migration speed, apoptosis_rate, lac_Secretion_Rate, Transition_Rate

Model Rules

- Initial Energy = 450
- If Energy > 445
 - Cycle
- If Energy < 445
 - Don't Cycle
- If Energy < 440
 - Move
- If Energy < 430
 - Die

Populate together

- **PhysiCell folder**
- make clean
- make data-cleanup
- make reset
- make list-projects
- make ode-energy-sample
- make

The Roadmap

- First, we will create the modal domain in the PMB
 - Config Basics
 - Microenvironment
 - Cells
- Create SBML on Copasi
- Integrate SBML to PhysiCell model

Config Basics

- Domain size
 - $X = [-500, 500]$
 - $Y = [-500, 500]$
 - $Z = [-10, 10]$
 - $dx, dy, dz = 20$
 - $Use_2D = true$
- Max-time = 1440 min
- Thread = your choice
- Save data :
SVG = 30 min,

PhysiCell Model Builder C:\Users\Furkan\Documents\GitHub\PhysiCell-model-builder\data\template.xml

File Config Basics Microenvironment Cell Types User Params

Domain (micron)

Xmin -500 Xmax 500 dx 20

Ymin -500 Ymax 500 dy 20

Zmin -10 Zmax 10 dz 20

☐ Virtual walls

Times

Max Time 1440 min

Diffusion dt 0.01 min

Mechanics dt 0.1 min

Phenotype dt 6 min

Misc runtime parameters

threads 8

output folder output

Save data: ☒ SVG every 30 min ☒ Full every 30 min

Initial conditions of cells (x,y,z, type)

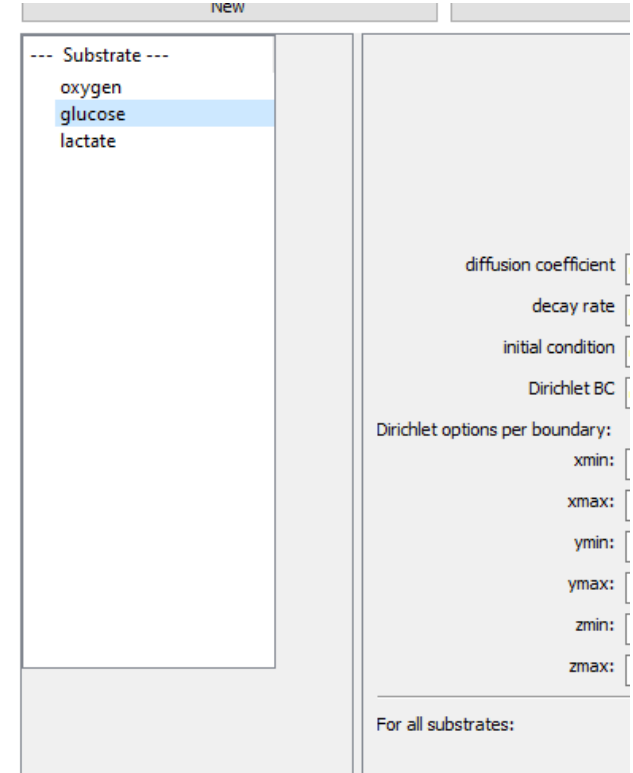
csv folder ./config

☐ cells.csv

Full = 30 min

Microenvironment

- Microenvironment Tab
- Let's add “oxygen”, “glucose”, “lactate”



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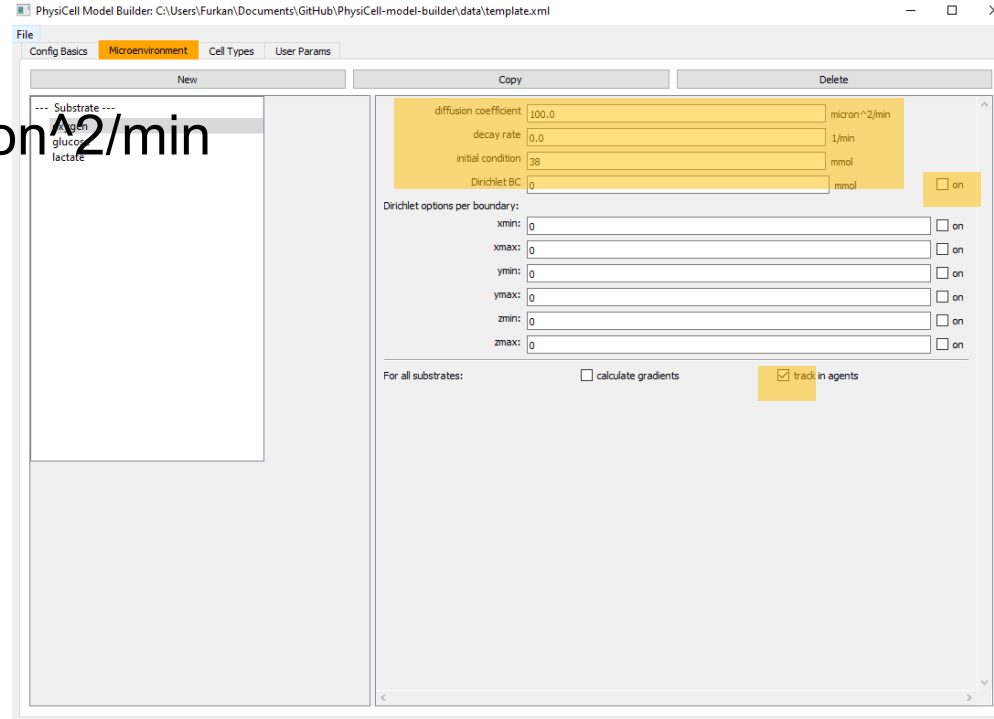
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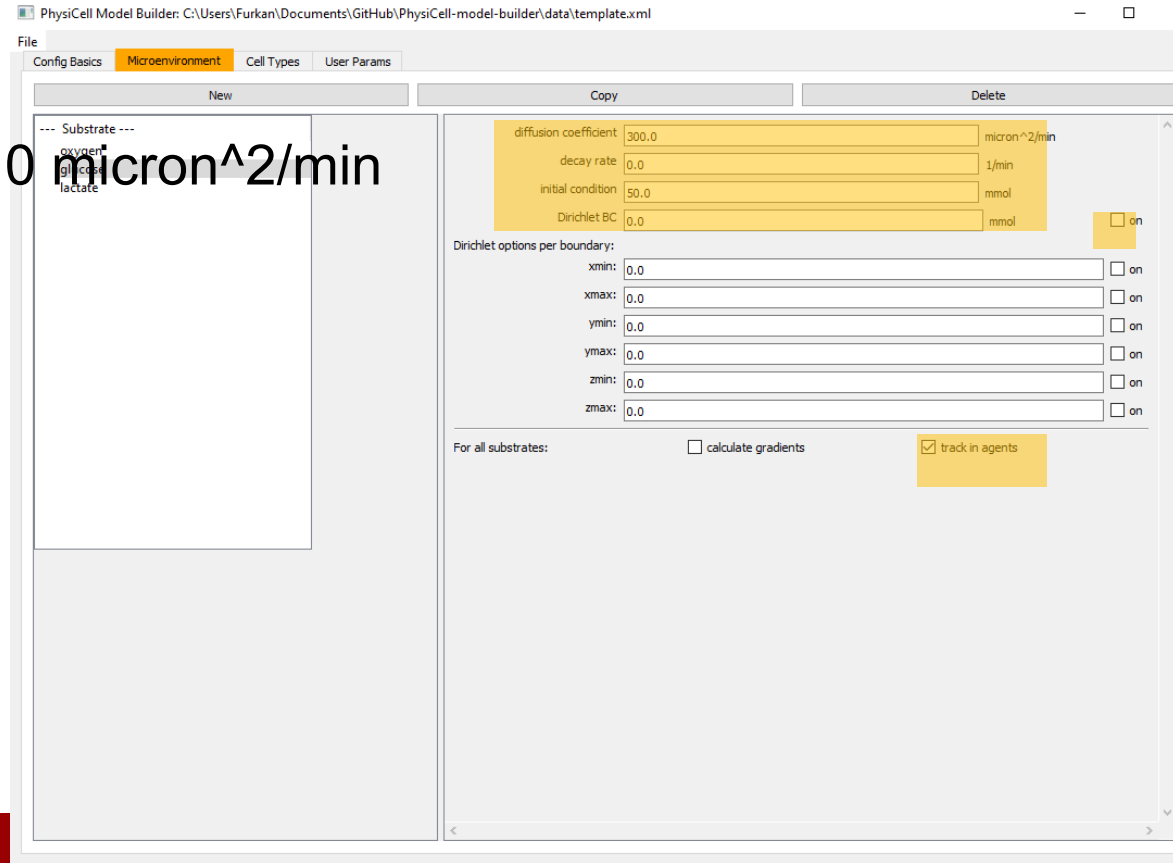
Microenvironment

- Oxygen
- Diffusion Coefficient = 100.0 $\mu\text{m}^2/\text{min}$
- Decay Rate = 0.0 1/min
- Initial condition = 38.0 mmHg
- Dirichlet = OFF
- Track in agents = ON



Microenvironment

- Glucose
- Diffusion Coefficient = 300.0 $\mu\text{m}^2/\text{min}$
- Decay Rate = 0.0 1/min
- Initial condition = 50.0 a.u
- Dirichlet = OFF
- Track in agents = ON



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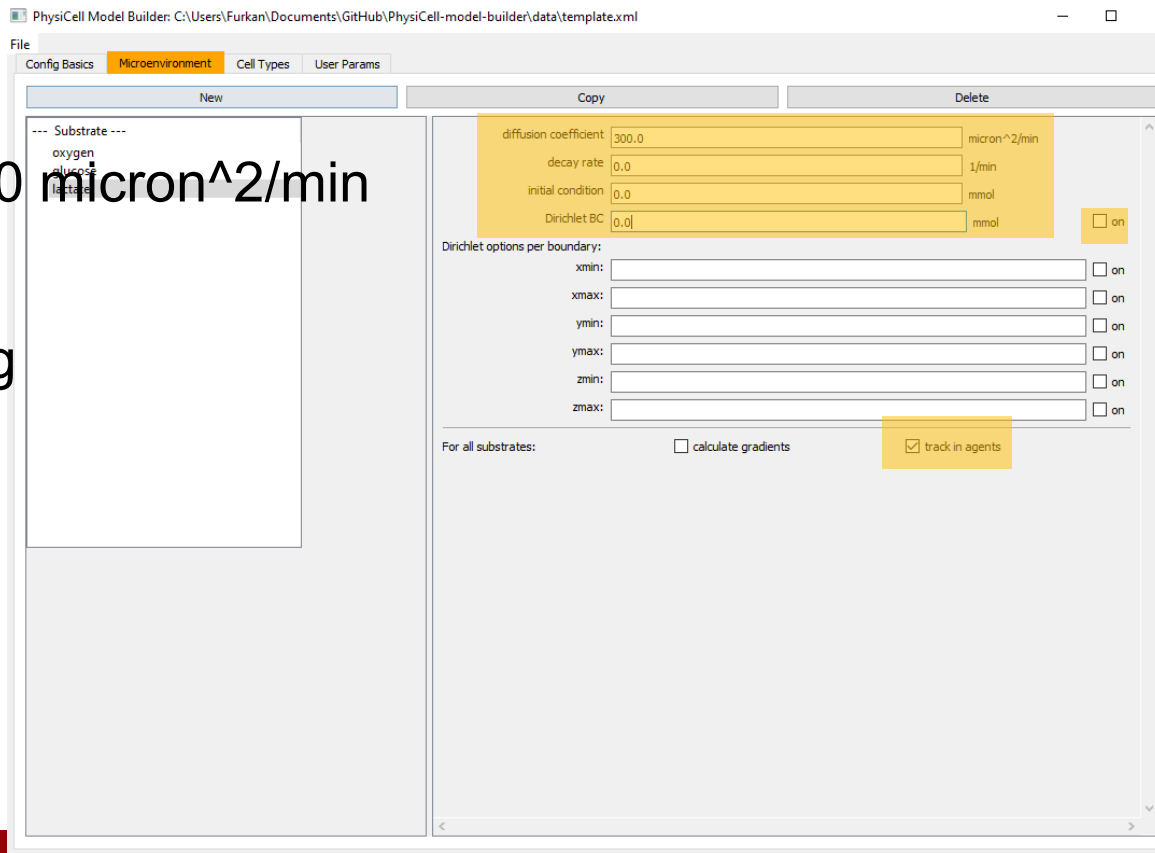
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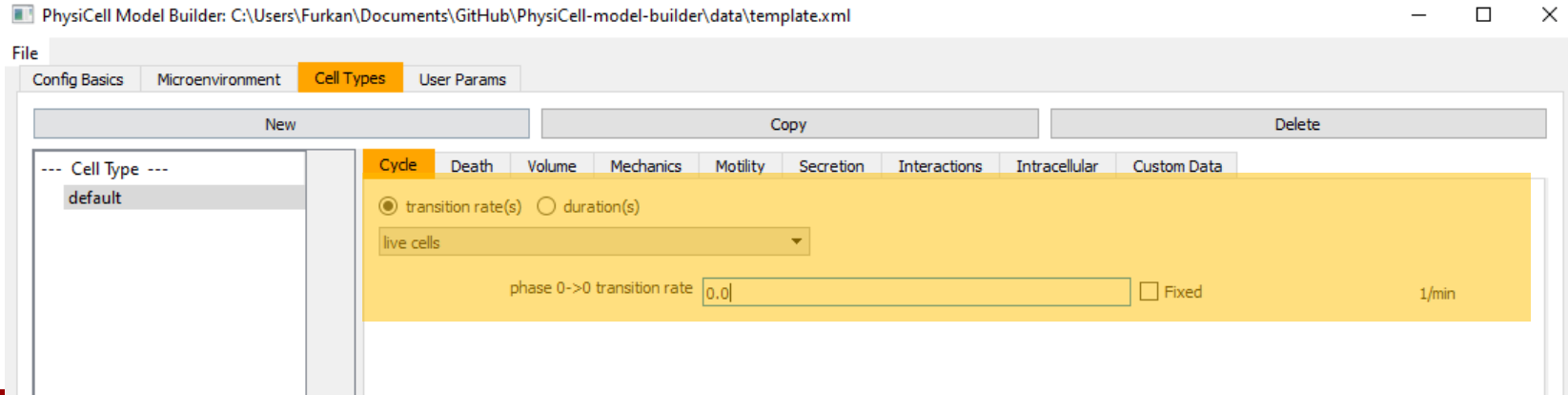
Microenvironment

- Lactate
- Diffusion Coefficient = 300.0 $\mu\text{m}^2/\text{min}$
- Decay Rate = 0.0 1/min
- Initial condition = 0.0 mmHg
- Dirichlet = OFF
- Track in agents = ON



Cell Type

- Only one type of cell in the name of “default”
- Cycle
 - Live Cells
 - Transition rate(s)
 - 0.0



Cell Type

- No Death

Config Basics Microenvironment **Cell Types** User Params

New Copy Delete

--- Cell Type ---
default

Cycle **Death** Volume Mechanics Motility Secretion Interactions Intracellular Custom Data

Apoptosis

death rate 0.0 1/min

☒ transition rate ☐ duration

phase 0->1 transition rate 0.0 ☐ Fixed min

phase 0 duration 516 ☒ Fixed min

unlysed fluid change rate 0.05 1/min

lysed fluid change rate 0 1/min

cytoplasmic biomass change rate 1.66667e-02 1/min

nuclear biomass change rate 5.83333e-03 1/min

calcification rate 0 1/min

relative rupture volume 2.0

Necrosis

death rate 0.0 1/min

☒ transition rate ☐ duration

phase 0->1 transition rate 0.0 ☐ Fixed 1/min

phase 1->2 transition rate 0.0 ☐ Fixed 1/min

phase 0 duration 0 ☒ Fixed min

phase 1 duration 86400 ☒ Fixed min

unlysed fluid change rate 0.05 1/min

lysed fluid change rate 0 1/min

cytoplasmic biomass change rate 1.66667e-02 1/min

nuclear biomass change rate 5.83333e-03 1/min

calcification rate 0 1/min

Cell Type

- No change in the Volume and Mechanics Tab

PhysiCell Model Builder: C:\Users\Furkan\Documents\GitHub\PhysiCell-model-builder\data\template.xml

File Config Basics Microenvironment **Cell Types** User Params

New Copy Delete

--- Cell Type ---
default

	Cycle	Death	Volume	Mechanics	Motility	Secretion	Interactions	Intracellular	Custom Data
total	2494								micron ³
fluid fraction	0.75								
nuclear	540								micron ³
fluid change rate	0.05								1/min
cytoplasmic biomass change rate	0.0045								1/min
nuclear biomass change rate	0.0055								1/min
calcification fraction	0								
calcified rate	0								1/min
relative rupture volume	2.0								

PhysiCell Model Builder: C:\Users\Furkan\Documents\GitHub\PhysiCell-model-builder\data\template.xml

File Config Basics Microenvironment **Cell Types** User Params

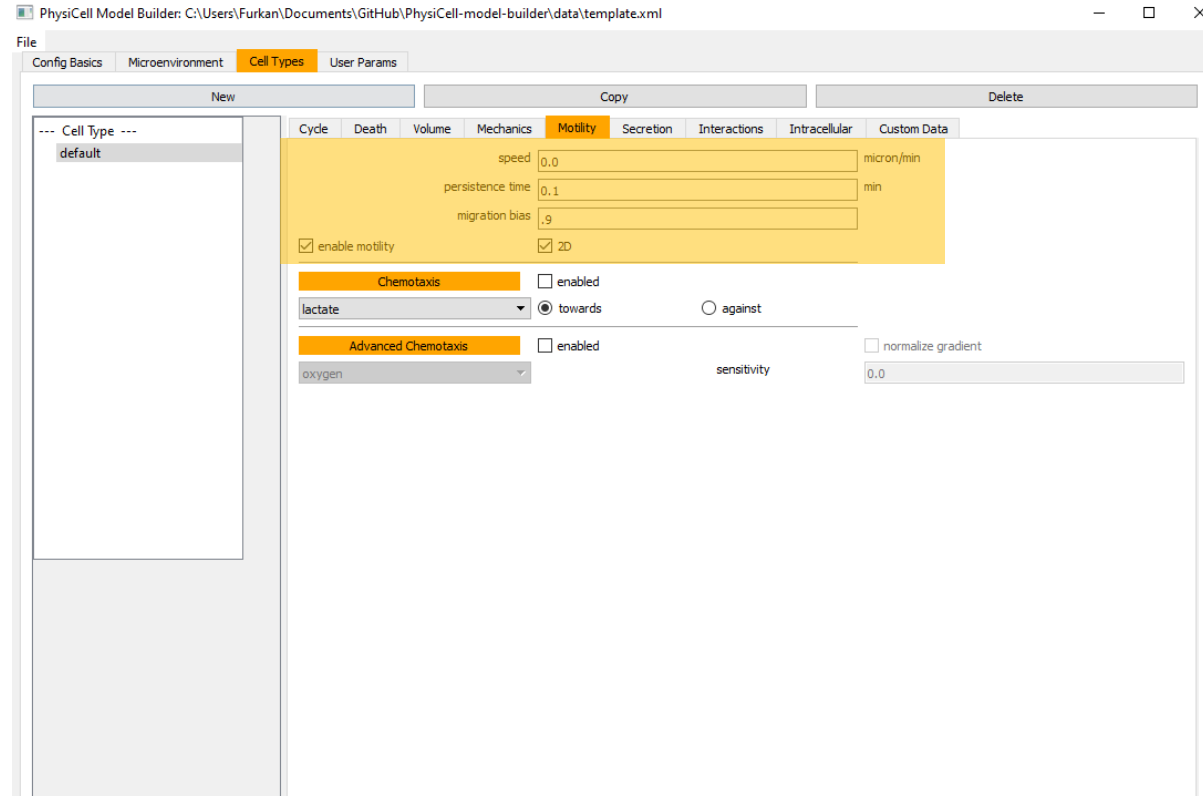
New Copy Delete

--- Cell Type ---
default

	Cycle	Death	Volume	Mechanics	Motility	Secretion	Interactions	Intracellular	Custom Data
cell-cell adhesion strength	0.4								micron/min
cell-cell repulsion strength	10.0								micron/min
cell-EM adhesion strength	4.0								micron/min
cell-EM repulsion strength	10.0								micron/min
relative max adhesion distance	1.25								
cell adhesion affinity	default								1.0
Options:									
relative equilibrium distance	1.8							<input type="checkbox"/> enable	
absolute equilibrium distance	15.12							<input type="checkbox"/> enable	micron
elastic constant	0.01								1/min
attachment rate	10.0								1/min
detachment rate	0.0								1/min

Cell Type

- Motility
- Speed = 0.0
- Persistence Time = 0.1
- Migration Bias = 0.9
- Enable-motility
- 2D = Yes



Cell Type : Secretion

- Oxygen Tab
- Uptake rate = 0.005

PhysiCell Model Builder: C:\Users\Furkan\Documents\GitHub\PhysiCell-model-builder\data\template.xml

File

Config Basics Microenvironment **Cell Types** User Params

New Copy Delete

--- Cell Type ---

default

Cycle Death Volume Mechanics Motility **Secretion** Interactions Intracellular Custom Data

oxygen

secretion rate 0.005 1/min

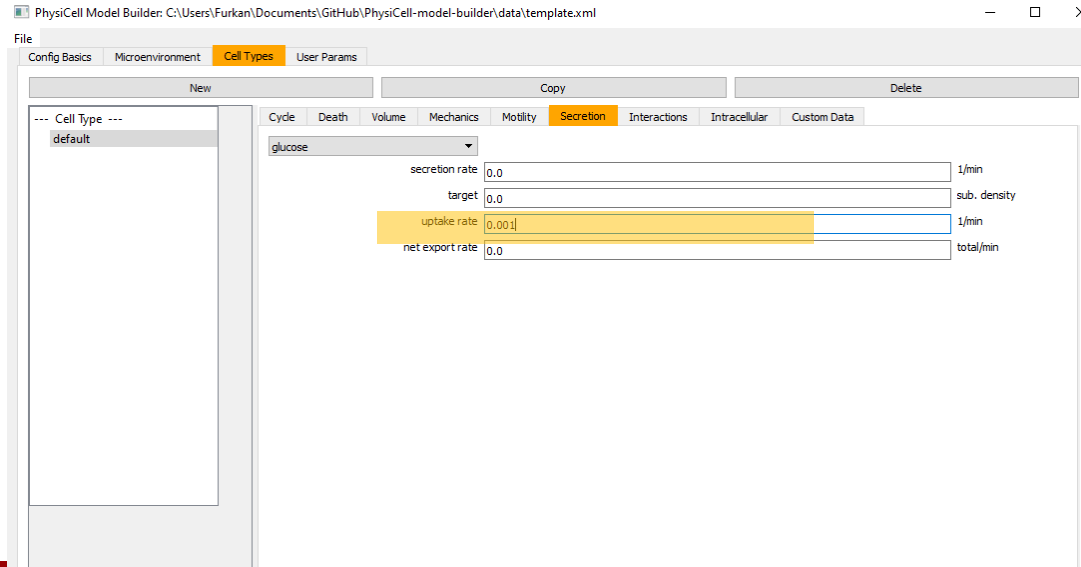
target 1 sub. density

uptake rate 0 1/min

net export rate 0 total/min

Cell Type : Secretion

- Glucose Tab
- Uptake rate = 0.001



Cell Type : Secretion

- Lactate Tab
- Secretion Target = 10.0

PhysiCell Model Builder: C:\Users\Furkan\Documents\GitHub\PhysiCell-model-builder\data\template.xml

File

Config Basics Microenvironment **Cell Types** User Params

New Copy Delete

--- Cell Type ---
default

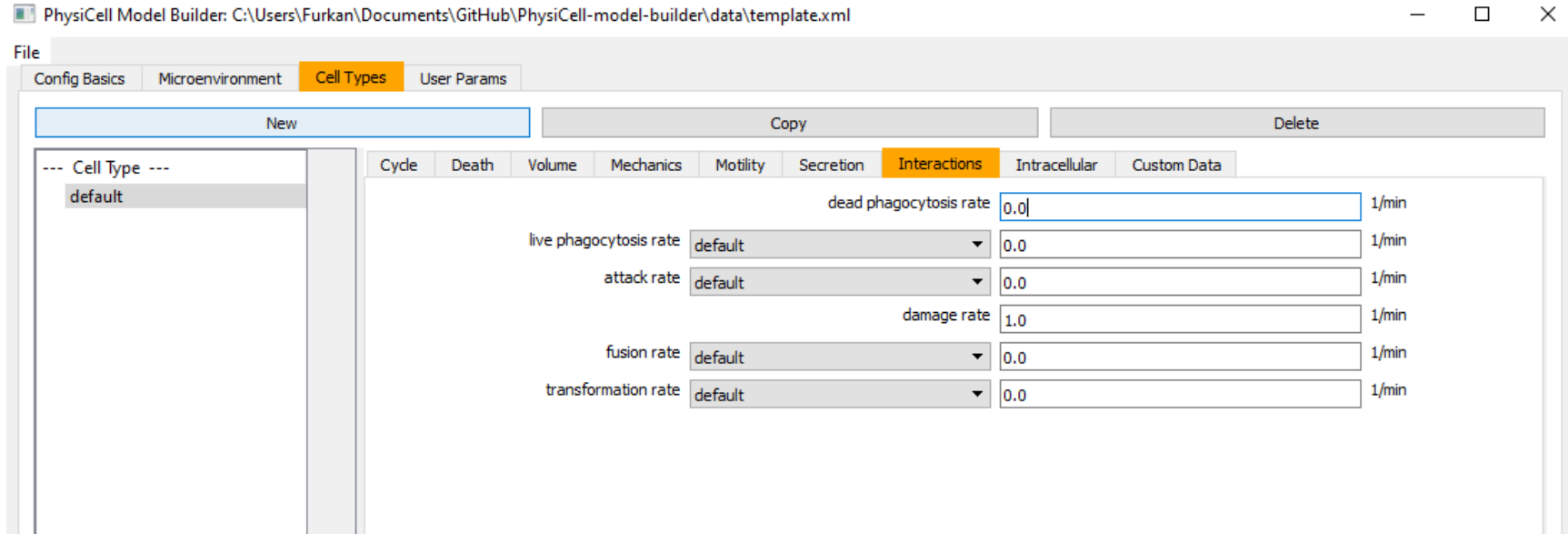
Cycle Death Volume Mechanics Motility **Secretion** Interactions Intracellular Custom Data

lactate

secretion rate	0.0	1/min
target	10.0	sub. density
uptake rate	0.0	1/min
net export rate	0.0	total/min

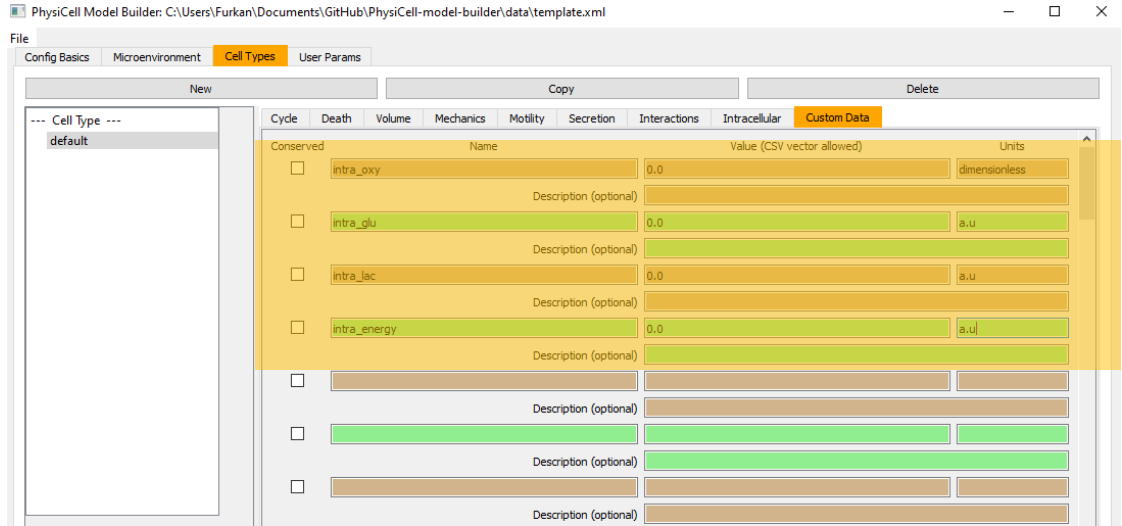
Cell Type

- No Interactions



Cell Custom Data

- We need to create intracellular data to save the data
- $\text{intra_oxy} = 0.0$
- $\text{intra_glu} = 0.0$
- $\text{intra_lac} = 0.0$
- $\text{intra_energy} = 0.0$



User Params

PhysiCell Model Builder: C:\Users\Furkan\Documents\GitHub\PhysiCell-model-builder\data\template.xml

File

Config Basics Microenvironment Cell Types **User Params**

Append 10 more rows

Clear selected rows

	Name	Type	Value	Units
<input type="checkbox"/>	initial_internal_oxygen	double ▾	0.8	mmHg
Description:				
<input type="checkbox"/>	initial_internal_glucose	double ▾	15	a.u
Description: initial number of cells (for each cell type)				
<input type="checkbox"/>	initial_internal_lactate	double ▾	0.0	a.u
Description:				
<input type="checkbox"/>	initial_energy	double ▾	450	a.u
Description:				
<input type="checkbox"/>		double ▾		
Description:				
<input type="checkbox"/>		double ▾		
Description:				
<input type="checkbox"/>		double ▾		
Description:				
<input type="checkbox"/>		double ▾		
Description:				



Save

- Let's check is it right

Let's Simulate

- But First
- Let's get rid of the all-intracellular related part
 - In the custom module
 - Browse through the setup tissue() function
 - Remove the inner code of the for loop
 - ♦ Starting with Line #166 to #183 (except assigning)
 - Remove the inner part of update_intracellular() function
 - ♦ Starting with Line #192 to #263
 - That's all
- CHECKPOINT - 1

Funding Acknowledgements



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The Common
Fund



leidos



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- National Science Foundation (1720625, 1818187)

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