

Identifying proteins and metabolic pathways associated with the neuroprotective response mediated by tibolone in astrocytes under an induced inflammatory model

Daniel Osorio^{1,2,3} Janneth Gonzalez² Andrés Pinzon³

¹Departamento de Ingeniería de Sistemas e Industrial
Facultad de Ingeniería, Universidad Nacional de Colombia

²Grupo de Investigación en Bioquímica Experimental y Computacional
Facultad de Ciencias, Pontificia Universidad Javeriana - Bogotá

³Grupo de Investigación en Bioinformática y Biología de Sistemas
Instituto de Genética, Universidad Nacional de Colombia

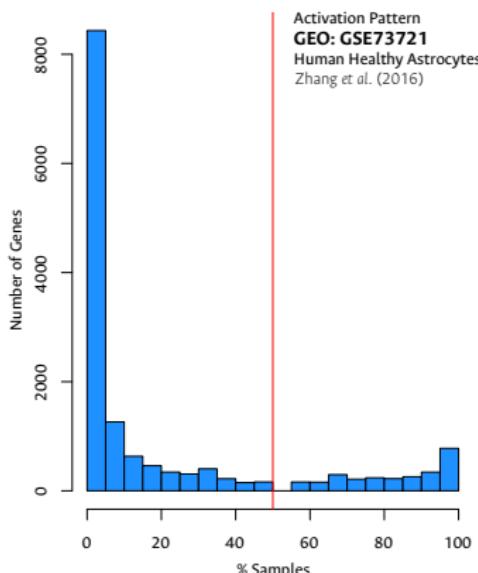
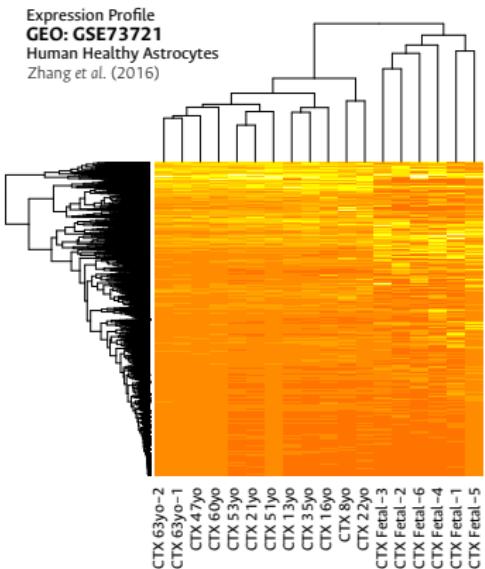
Universidad Nacional de Colombia, November 2016

Objectives:

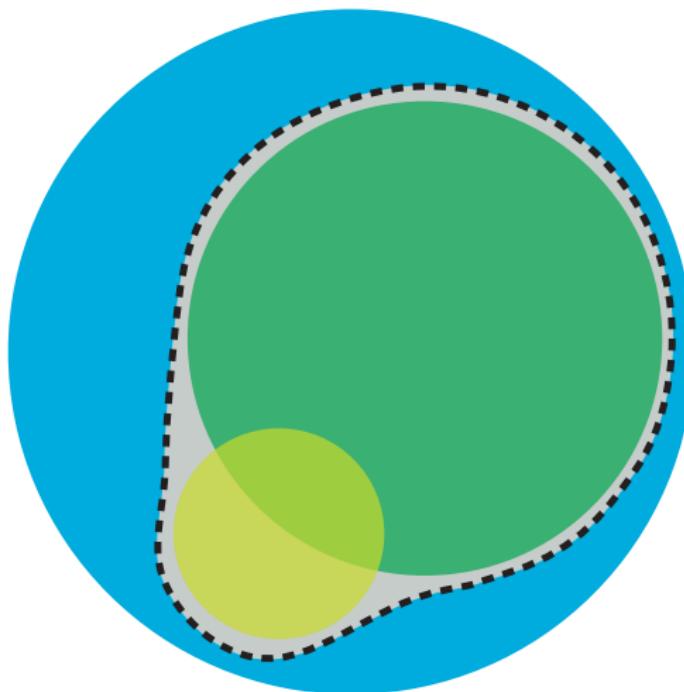
To identify proteins and metabolic pathways involved in the neuroprotective effects of tibolone in human astrocytes based in metabolic scenarios comparation we set:

- ▶ Build a tissue specific computational model of astrocytes metabolism using gene expression data integration.
- ▶ Evaluate the effects caused by the increase of free fatty acids and tibolone presence in astrocytes metabolism.
- ▶ Determine metabolic pathways and relevant functional products in response to steroid tibolone through systems biology approximations.
- ▶ Evaluate the importance of proteins and metabolic pathways previously identified on the dynamics of the metabolic model.

Human Astrocytes Gene Expression Data



Mapping Reactions



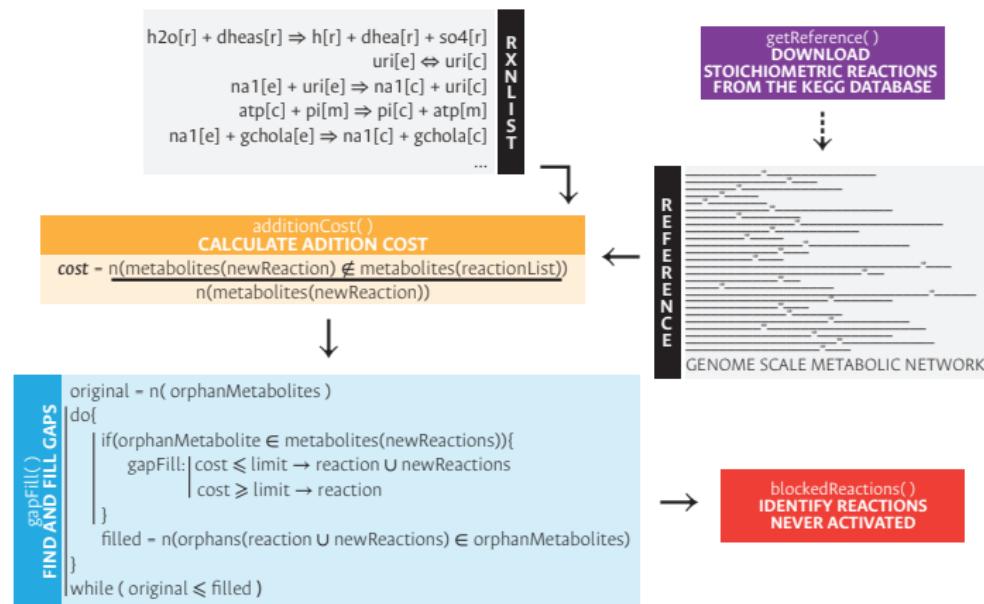
Software Development



'g2f' Package

An R Package to Find and Fill Gaps for genome-scale metabolic networks
 Kelly Botero, Daniel Osorio, Janneth Gonzalez and Andres Pinzón-Velasco.

Language: R
 Stable: CRAN
 Development: gibbslab/g2f
 License: GPL-2
 Binaries: Windows - Linux - Mac



Software Development

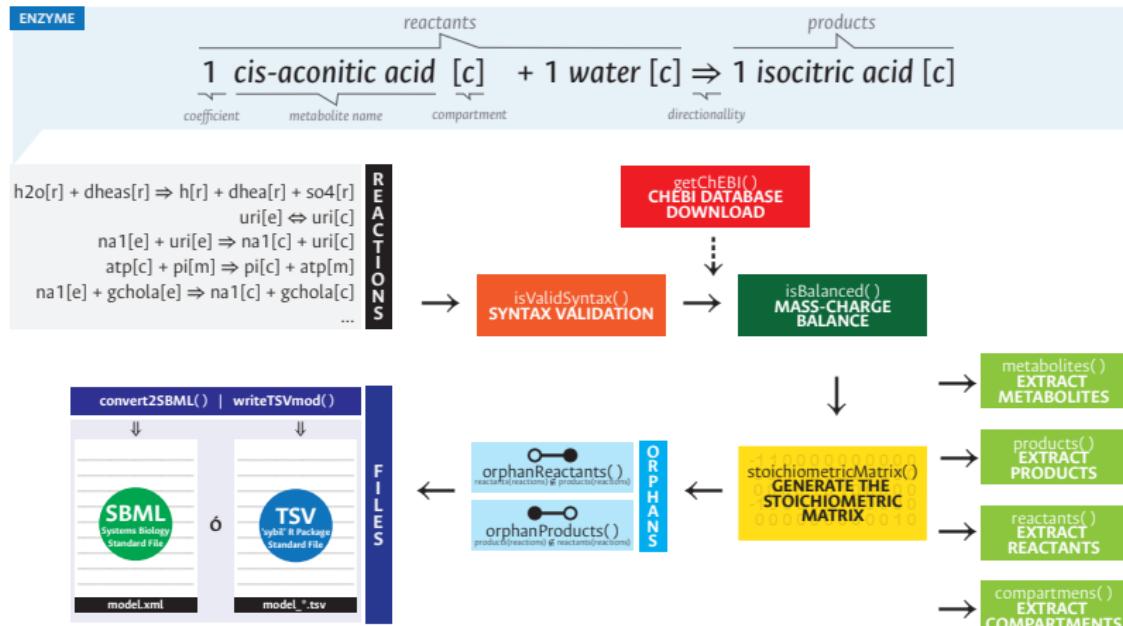


‘minval’ Package

An R Package for MINimal VAIdation of stoichiometric reactions

AN R Package for MINIMAL VI REGRESSION OF
Daniel Osorio, Janneth González and Andrés Pinzón-Velasco

Language: R
Stable: CRAN
Development:  gibbslab/minerva
License:  GPL-2
Binaries: Windows - Linux - R



Software Development



'exp2flux' Package

An R Package to convert expression data to FBA fluxes
Daniel Osorio, Kelly Botero, Janneth Gonzalez and Andres Pinzón-Velasco.

Language: R

Stable: CRAN

Development: [gibbslab/exp2flux](#)

License: [GPL-2](#)

Binaries: Windows - Linux - Mac

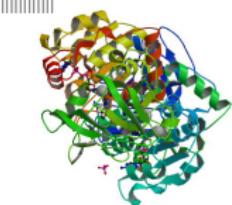
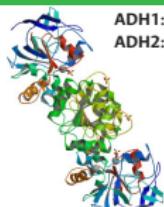
E.C: 1.1.1.1



1.1.1.1

ADH2

ADH1



(ADH2 or ADH1)

sum (ExprADH2 + ExprADH1)

E.C: 3.4.21.5



3.4.21.5

IDE.A

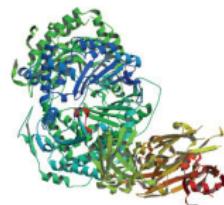
IDE.B

IDE.C

IDE.A:

IDE.B:

IDE.C:



GPR

(IDE.A and IDE.B and IDE.C)

min (ExprIDE.A, ExprIDE.B, ExprIDE.C)

GENE EXPRESSION
DATA



exp2flux()
CONVERT GENE
EXPRESSION DATA
TO FBA FLUXES



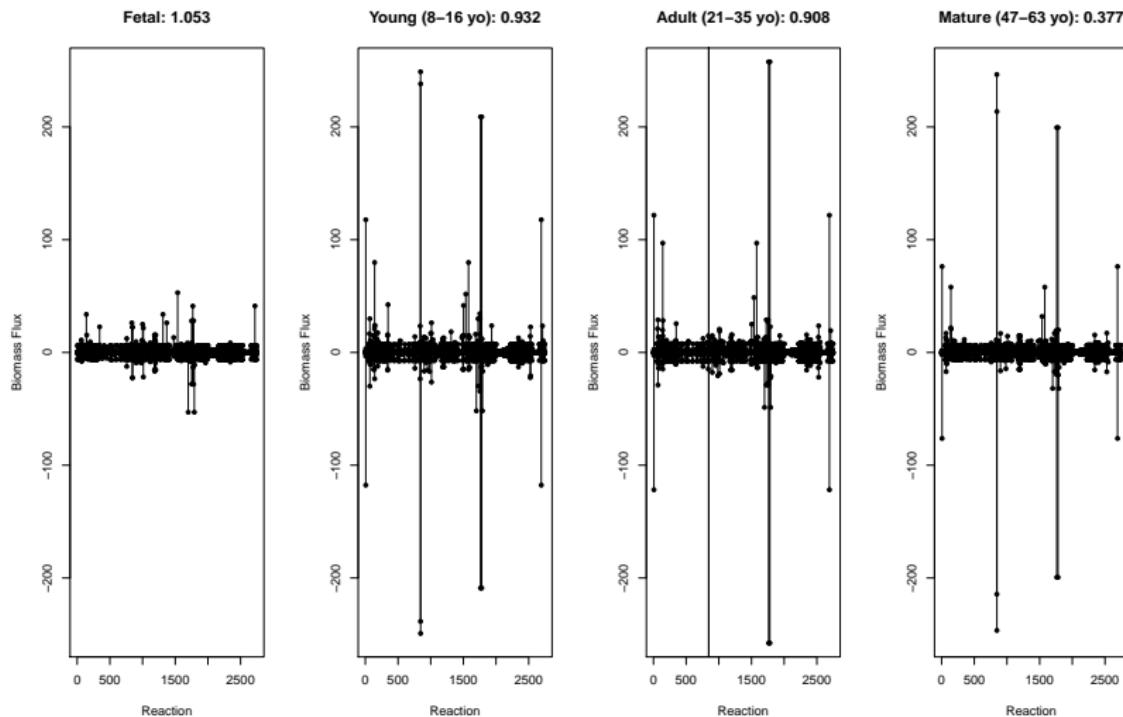
CONSTRAINED
METABOLIC MODEL



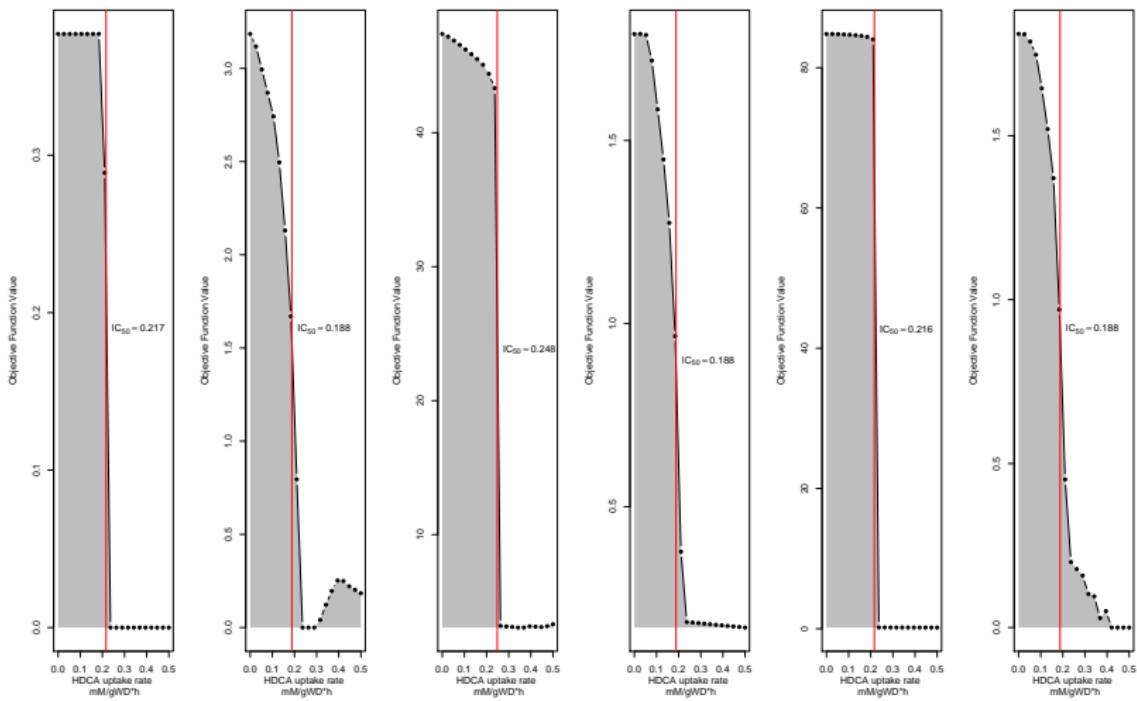
fluxDifferences()
COMPUTE FOLDCHANGE
OF FLUXES BETWEEN
METABOLIC SCENARIOS

METABOLIC MODEL
WITH GPR

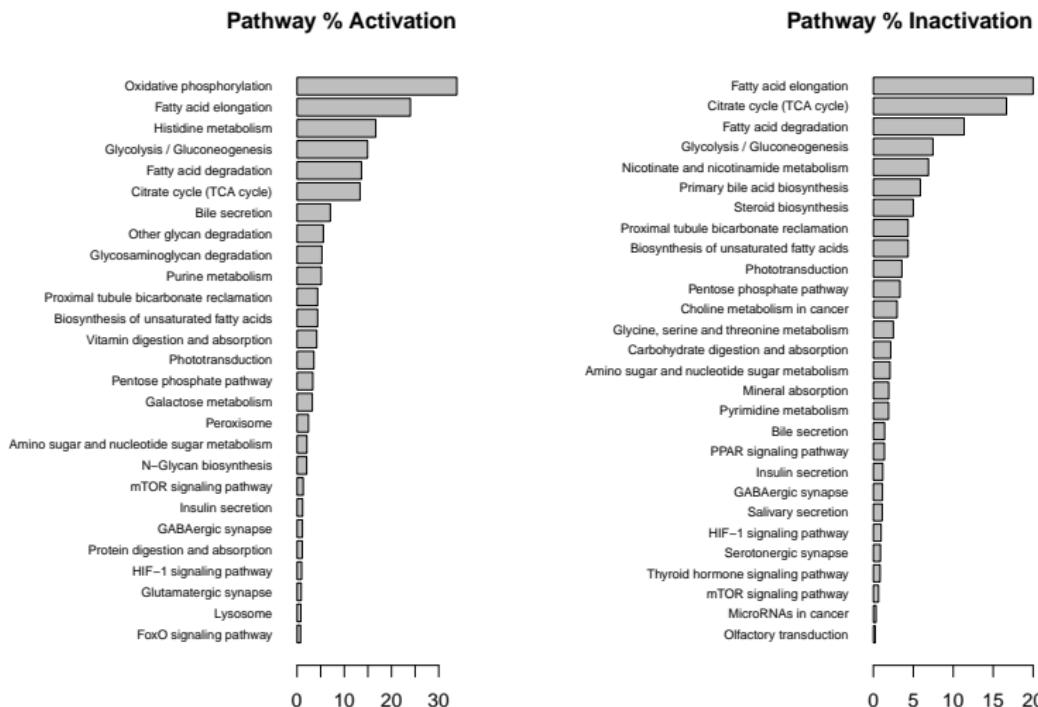
Age Related Metabolic Changes in Astrocytes



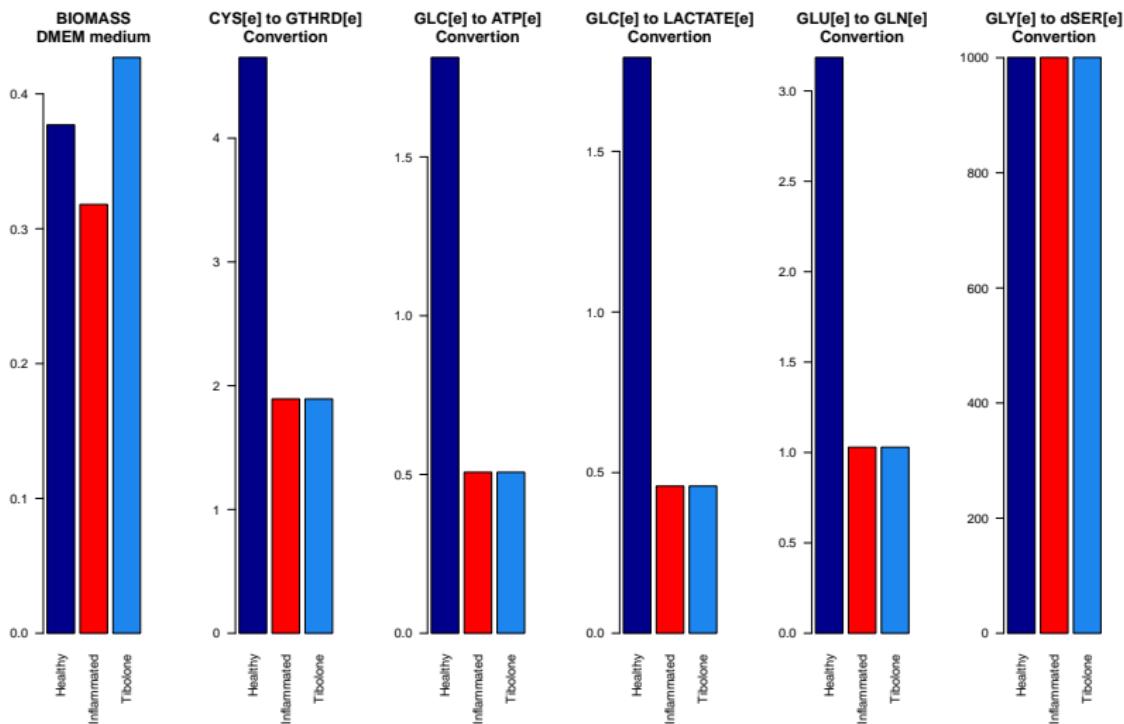
$$IC_{50} = 0.208 \pm 0.024 \text{ mMgDW}^{-1}\text{h}^{-1}$$



Inflammation Related Metabolic Changes in Astrocytes

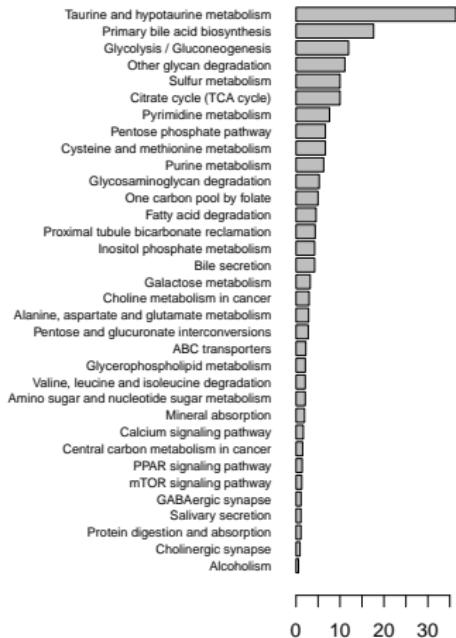


Tibolone Effects in Inflamed Astrocytes

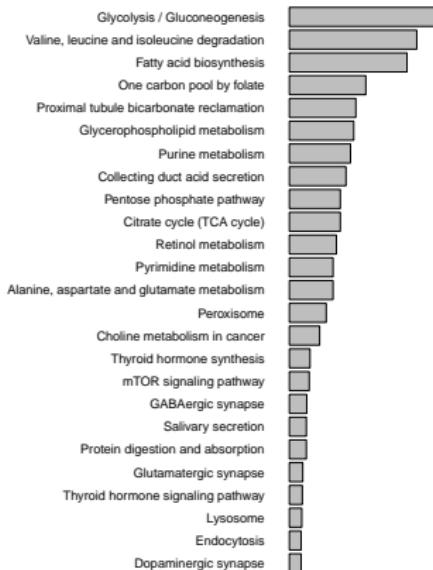


Tibolone Metabolic Changes in Inflamed Astrocytes

Pathway % Activation



Pathway % Inactivation



Advances of this work were presented as:

Metabolic inflammation effects over the gliotransmitters release in mature astrocytes: a network-based approach.

Daniel Osorio MSc., Janneth Gonzalez PhD., Andrés Pinzón-Velasco PhD.
Bioinformatics and Computational Systems Biology Lab, Universidad Nacional de Colombia.



at: _____



CDMX, México
Short Talk



Barcelona, España
Poster

ICGEB Course on Bioinformatics and Computational Neuroscience



Pontificia Universidad Javeriana
5 - 8 October - Bogotá, Colombia

Bogotá, Colombia
Short Talk

This study is under development at the:



Bioinformatics and Computational Systems Biology Lab

Institute for Genetics - Universidad Nacional de Colombia

CONTACT:

Daniel Osorio
dcosorioh@unal.edu.co

Andrés Pinzón PhD
ampinzonv@unal.edu.co