



# Use of Constraint Based Methods for Analysis of Senescence

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# Senescent Cells

Unable to replicate anymore.

Associated with aging.

Caused by different types of internal or external stress.

Telomere shortening is one common senescence cause.

Have a multi-component senescence-associated secretory phenotype (SASP).

Phenotype is dynamic and depends on cell and stress type.

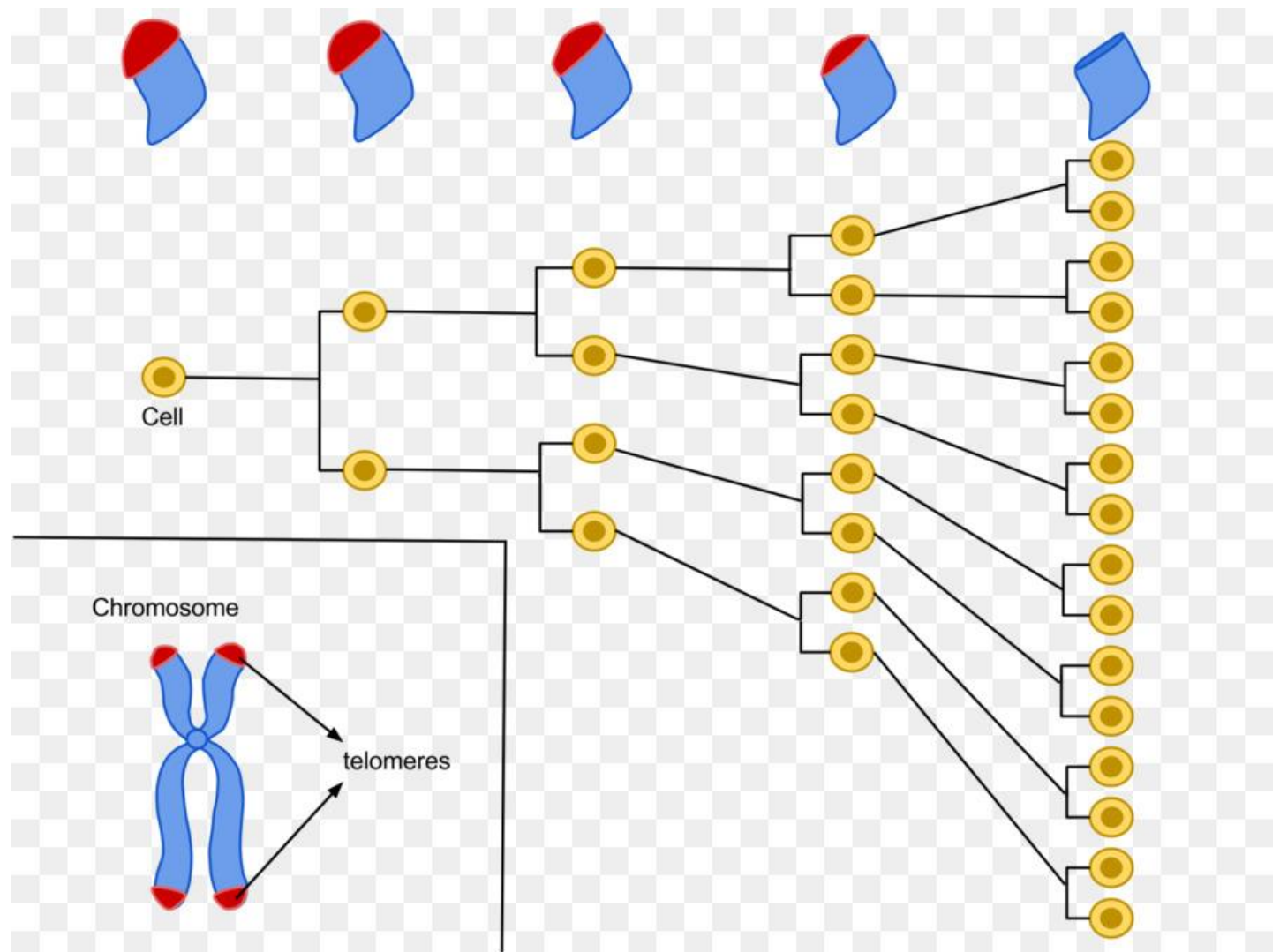


Figure 1: Telomere shortening as a common cause of senescence. Retrieved from: [https://en.wikipedia.org/wiki/Cellular\\_senescence](https://en.wikipedia.org/wiki/Cellular_senescence)

## Benefits:

Protection of Organisms from cancer.

Improvement of specific biological processes(wound healing, embryonic structure formation)

## Detriments:

Senescence-associated secretory phenotype(SASP) has a detrimental effect on surrounding cells.

Linked to age-related diseases

Wiley, C., & Campisi, J. (2016). From Ancient Pathways to Aging Cells—Connecting Metabolism and Cellular Senescence. *Cell Metabolism*, 23(6), 1013-1021. doi: 10.1016/j.cmet.2016.05.010

# Benefits and Detriments of Senescence



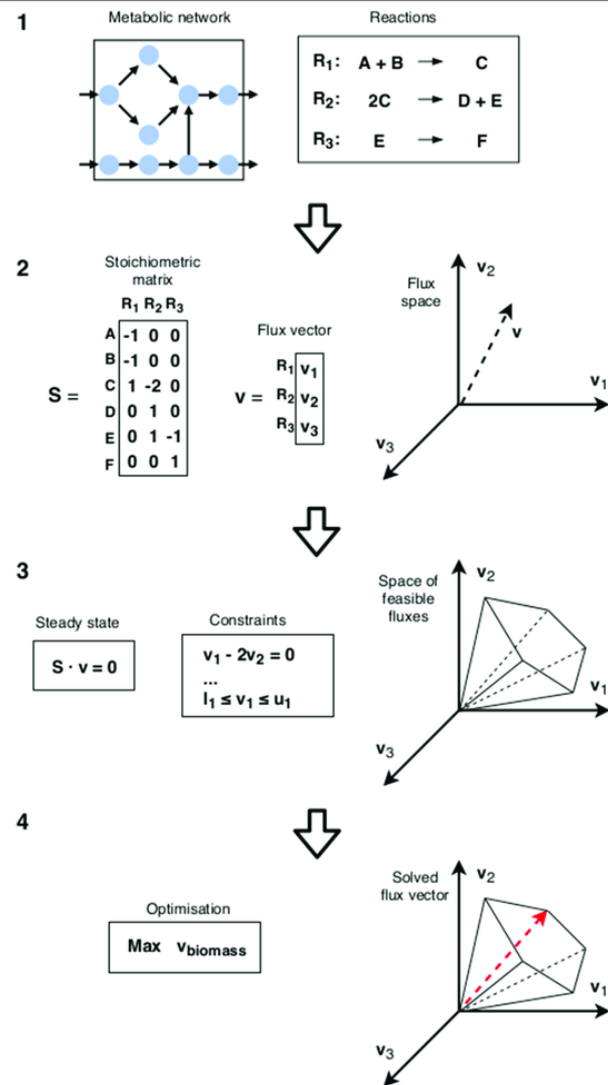


Figure 3: Visualization of Flux Balance Analysis. Retrieved from: <https://www.frontiersin.org/articles/10.3389/fams.2019.00018/full>

# COBRA

Constraint-Based Reconstruction and Analysis(COBRA) methods can be used to analyze the metabolic models of non-senescent and radiation-induced senescent human diploid fibroblast cells (WI-38).

COBRA imposes a steady-state mass balance constraint which keeps the concentration of all the metabolites constant.

These constraints mathematically describe a multidimensional solution space of the possibly steady-state flux distributions of the model.

# Monte Carlo Sampling

Commonly used COBRA method.

Whole flux space is sampled in a uniform fashion yielding a big number of flux vectors that collectively map out a solution space.

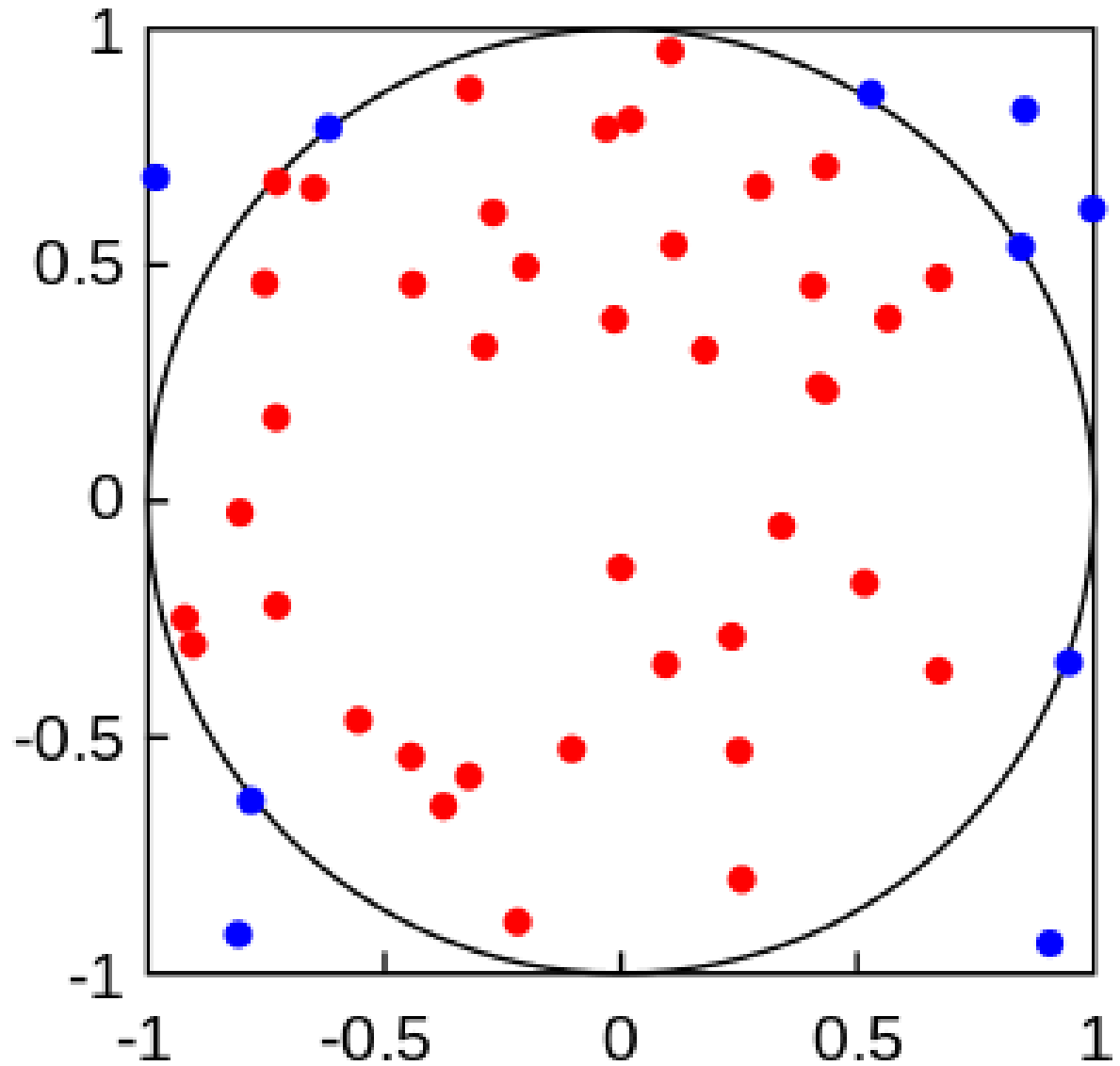


Figure 4: Visualization of Monte Carlo Sampling. Retrieved from: [https://en.wikipedia.org/wiki/Monte\\_Carlo\\_integration](https://en.wikipedia.org/wiki/Monte_Carlo_integration)

# Expectation Propagation

Is a similar method to Flux Space Sampling which is based on Expectation Propagation (EP) equations and provides a probability distribution for each reaction flux.

EP provides an analytical approximation to Monte Carlo Sampling.

EP has much lower computation time and yields similar results to Monte Carlo Sampling.

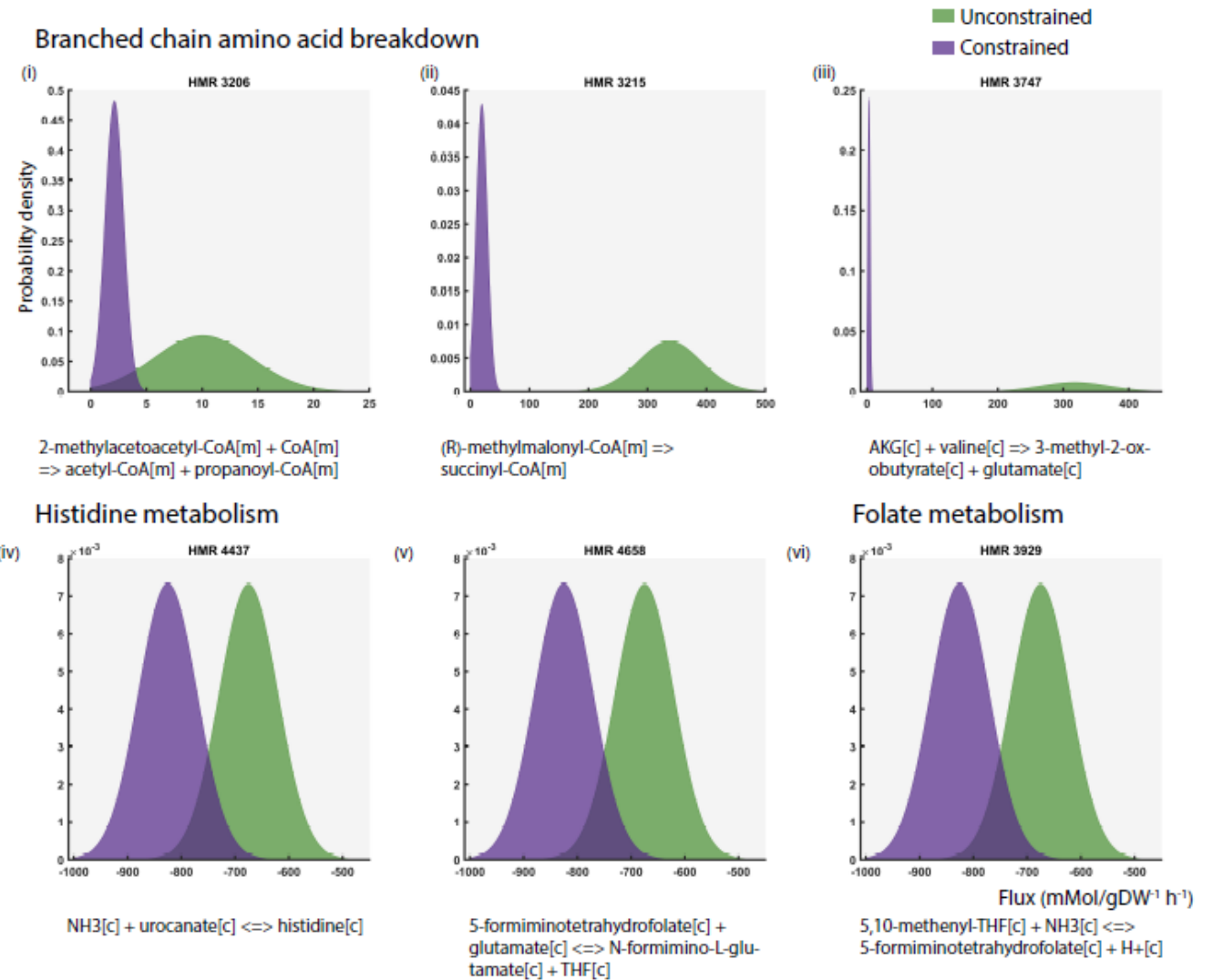


Figure 5: Probability distribution of reaction flux of different reactions. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.09.14.296145v1>



# ComMet

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ComMet is a method to compare metabolic states between metabolic networks.

ComMet uses EP for sampling which means it can be used to analyze flux rates of the metabolic model of non-senescent and radiation-induced senescent human diploid fibroblast cells (WI-38).



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