Modelling the Electron Transfer in E.Coli Using Kappa

# Introduction:

The sub-processes are as follows:

**Sub-process: Corresponding Kappa File:**

1. Glucose -> TCA cycle -> Quinol 1\_TCA.ka

2. Quinol -> NapC 2\_NapC.ka

3. Electron transfer between NapC, NapAB, NrfA and MtrA 3\_MtrA.ka

4. MtrA -> MtrB -> MtrC 4\_MtrABC.ka

5. MtrC -> Unsoluble Iron (including the Flavins) 5\_UFe.ka

# 1\_TCA.ka:

Glucose -> TCA cycle -> QH2

## Agents and Tokens

**# Tokens # # Agents #**

%token: Glucose %agent: TCA(glucose~0~1)

%token: NADH %agent: ComplexI(FMN~0~H)

%token: succinate %agent: ComplexII(FAD~0~H)

%token: Quinol

There is a linear relation between the amount of glucose and the amount of Acyl-CoA in the cell except when the amount of glucose is less than 0.5 mM or more than 5.5 mM. Acyl-CoA has a default minimal amount of 0.14mM and cannot go over 0.4mM. (1) Since Acyl-CoA is mainly used in the TCA cycle, we assume linear relation between the amount of glucose and the number of ‘running’ TCA cycles. We estimate the amount of running TCA cycle by dividing the amount of Acyl-CoA in the cell (each TCA cycle needs two molecules of Acyl-CoA per molecule of glucose).

The token Quinol refers to coenzyme Q10 (aka ubiquinone).

## Rules

'TCA consumes Glucose'

'TCA produces NADH and succinate'

The products from the TCA cycle per molecule of glucose are 6xNADH and 2xFADH. (2)

NADH binds to Complex I via FMN which takes the electrons from NADH. The electrons are then passed to a series of iron-sulphur clusters which we ignore in the model. The electrons leave Complex I and are taken by the ubiquinone. (3)

Succinate in the TCA cycle 'binds' to FAD in Complex II. Then Complex II reduces the quinol. (4)

#In fact, NADH binds to Complex I, but we model NADH as a token in order to simplify the model.

# 2\_NapC.ka

Quinol -> NapC

## Agents

# Number of NapC-s per cell???

# NapC has 4 hemes, so we assume it can take up to 4 electrons

## Rules

# The rate at which a Quinol (gives electrons/binds to) to NapC(carry~0) and NapC(carry~2) is the same, i.e. NapC(carry~0) has the same chance of (receiving electrons from/binding to) a Quinol as NapC(carry~2).

# 3\_MtrA.ka

Electron transfer between NapC, NapAB, NrfA and MtrA

# 4\_MtrABC.ka

4A. MtrA -> Fe soluble &

4B. MtrA -> MtrB -> MtrC

Problem: MtrC subsystem is assuming unlimited electrons. If assumption is correct this just sets a lower limit on the output of this sub-system. If this is the case, how can correctness be verified? Potentially the MtrA -> Fe soluble part could be verified somehow.

## Agents and Tokens

Each unit of soluble iron takes a single electron.

There are 75 MtrC-s. (5)

Can’t find exact heme structure information for MtrA. Assume it can connect to either MtrBC or NapC and simultaneously to a single Fe. If it can actually connect to multiple Fe’s, like MtrC, the difference should be able to be corrected by a slightly different kOff.

Will model such as non-full mtrA is deleted and full mtrA is added to replace it at some constant rate. Not yet sure if this rate should be limiting step or not.

## Rules

MtrC stays attached to MtrB. (6) There are 75 MtrC-s so there’ll be 75 relevant MtrB-s. There must be a better source than (6) for the fact that MtrC stays attached, but while it seems to be tacitly assumed in many papers I can’t [seem to find a direct source for the fact.](slot:)

We assume electrons can travel instantly and without effort between all 10 hemes of MtrC. (7) one heme picks up electrons from MtrA, one heme gives electrons to Fe2O3, and 2 hemes give electrons only to soluble agents. These 4 can work concurrently. Input will be made arbitrarily fast based on assumption. (5)

# 5\_UFe.ka

MtrC -> Unsoluble Iron (including the Flavins)

## Agents and Tokens

There are 2100 MtrA-s. (5)

Each Flavin can take 1 or 2 electrons. (8)

Since we’re talking about nano/microscale pieces of Fe2O3 and not individual molecules, assume these will reduce as much as they can. Since we are adding flavins artificially, number can be varied. Could go between 0 and 1uM to match with paper (9).

## Rules

Off rates are proportional to number of electrons transferred – this one might be wrong, but not sure how to get flavin Off rate otherwise.

Electron transfer rates are at least 7/8 orders of magnitude bigger than kOn rates. Argument based on mEv of electron kinetics translated into speed compared to size of mtrC and to number of electrons transferred per second per cytochrome. Rough estimate, but should show the required difference in speed nonetheless. However it is unclear if the electron transfer itself is the longest part of the kOff process.

The system MtrC – Fe2O3 is considered to be bottlenecked for the insoluble iron output. (5) This implies that the rate at which electrons are available to MtrC might be irrelevant, so we assume they are infinite.

Again, as in 4\_MtrABC.ka we assume that electrons can travel instantly and without effort between all 10 hemes of MtrC.

From (5) we see that despite increasing number of iron particles by a huge amount, rate of electron transfer increases only by 2.5. Possible bottlenecks are number of electrons that reach mtrC or kOff between mtrC and Fe2O3 (because kOn should be proportional to number of items). But (9) shows that adding flavins increases the transfer rate significantly, this means that the amount of available electrons cannot be the bottleneck, therefore kOff must be it. Simulation shows that in order to fit the Jensen results kOff/kOn ~ 10000**.**

From (9) we also see the exact effect of adding flavins isn’t linear in the number of flavins either. Here the bottleneck comes from the small number of hemes from which the flavins can get the electrons(75 \* 2). Thus the flavin-mtrC kOf can be modelled to respect these curves. The determined value is ~ 100 times more frequent than mtrC-Fe2O3 Off. This fact is somewhat supported by (7), which says fast decoupling between flavins and mtrC is to be expected.

## VERIFICATIONS:

Reduction of Fe2O3 with only mtrC is ~10x slower than Shewanella. (5) The model predicts that 0.2 micromoles of flavins would be needed to increase reduction 10x. This shows that external flavin production in Shewanella is within 0.1 – 0.8 micromoles. Prediction is within a factor of 4 of reality.

Going from normal shewanella (0.1 – 0.8 micromoles of flavin) to 12 micromoles of flavin only incrases transfer rate 4-5 fold. (10) This means a bottleneck is hit. While the model can’t handle a simulation with 12 micromoles of flavin, the following behaviour can be observed:

This clearly shows that the gains are becoming logarithmically small at a rate approx 3-4 times that of 0.5 micromoles. This is consistent with the expected behaviour.

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