E.coli Energy Subsystem

The main method by which energy is generated in *E.coli* is by coupling the flow of electrons in membranes to the creation of a membrane-based proton-motive force. This proton-motive force is used by ATP synthase (ATPS4rpp) to convert adenosine diphosphate (adp_c) to adenosine triphosphate (atp_c). In *E.coli* the electrons flow from primary electron donors to terminal electron acceptors through a series of electron carrier proteins and a class of lipids called quinones that are located in the lipid phase of the membrane (in the models to be discussed they are located in the cytoplasmic space).

A shown in Figure 1 the basic structure of the electron transport chain includes the electron donors, dehydrogenases, a quinone pool, oxidases/reductases, and electron acceptor. The electron donors are low electrode potential metabolites that can transfer their electrons to a dehydrogenase with a high electrode potential. The electrons are then transferred to quinone that have a higher electrode potential than the dehydrogenases. The electrons are then transferred to either a higher electrode potential oxidase (aerobic) or a reductase (anaerobic). The final step is to transfer the electrons to the electron acceptors which will have higher electrode potentials than the oxidases/reductases. In this final step, some but not all of the oxidases/reductase serve as proton pumps that create the proton-motive force required for ATP synthase to convert adp_c to atp_c.

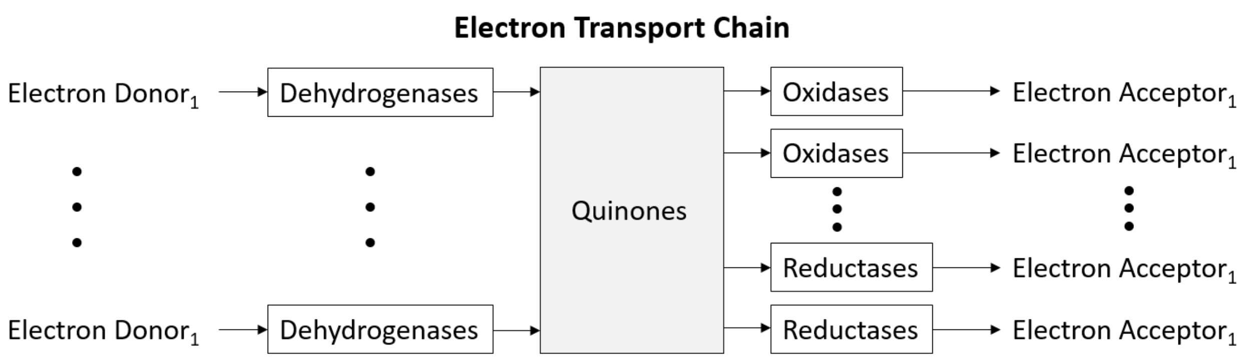

Figure 1. Electron transport chain

There are three different types of quinones present in *E.coli*, they include; **ubiquinone**, **menaquinone**, and **demethylmenaquinone**. The ubiquinone pools include ubiquinone-8 (q8_c) and a reduced version called ubiquinol-8 (q8h2_c) which carries the two extra electrons and protons. The menaquinone pool include menaquinone- 8 (mqn8_c) and its reduced version menaquinol-8 (mql8_c). Finally, the demethylmenaquinone pool include 2-Demethylmenaquinone 8 (2dmmq8_c) and the reduced version 2-Demethylmenaquinol 8 (2dmmql8_c). Experimentally, it has been shown that under aerobic conditions the ratio of quinones is 60% ubiquinone, 3% menaquinone, and 37% demethylmenaquinone. For anaerobic growth on nitrate the ratio is 0% ubiquinone, 30% menaquinone, and 70% demethylmenaquinone. For anaerobic growth on fumerate or DMSO the ratio is 10% ubiquinone, 70% menaquinone, and 16% demethylmenaquinone.[1]

The primary electrons donors in *E.coli* include; nicotinamide adenine dinucleotide – reduced (nadh_c), nicotinamide adenine dinucleotide phosphate – reduced (nadph_c) , formate (for_p), succinate (succ_c), pyruvate (pyr_c) , D-Lactate (lac__D_c), L-Lactate (lac__L_c), glycerol 3-phosphate (glyc3p_c), and hydrogen (h2_c). These electron donors interact with a dehydrogenase complex which removes electrons and starts them on a path through the electron transport chain.

The dehydrogenases and other reactions that interact with the quinone pool that are found in the *E.coli* models are shown below. This includes all reactions interacting with the quinone pools since these reactions can either reduce or oxidize quinone metabolites changing the pool creating an impact to the energy producing capabilities of the electron transfer chain.

Ubiquinone Dehydrogenases

Electron Donor	***Reactions***	***Reaction Names***
dhor__S_c	DHORD2	Dihydoorotic acid dehydrogenase (quinone8)
for_p	FDH4pp	Formate dehydrogenase (quinone-8) (periplasm)
glyc3p_c	G3PD5	Glycerol-3-phosphate dehydrogenase (ubiquinone-8)
glc__D_p	GLCDpp	Glucose dehydrogenase (ubiquinone-8 as acceptor) (periplasm)
glyclt_c	GLYCTO2	Glycolate oxidase
h2_c	HYD1pp	Hydrogenase (ubiquinone-8: 2 protons) (periplasm)
lac__L_c	L_LACD2	L-Lactate dehydrogenase (ubiquinone)
lac__D_c	LDH_D2	D-lactate dehydrogenase
mal__L_c	MDH2	Malate dehydrogenase (ubiquinone 8 as acceptor)
nadh_c	NADH16pp	NADH dehydrogenase (ubiquinone-8 & 3 protons) (periplasm)
nadh_c	NADH5	NADH dehydrogenase (ubiquinone-8)
nadph_c	NADPHQR2	NADPH Quinone reductase (Ubiquinone-8)
pyr_c	POX	Pyruvate oxidase
succ_c	SUCDi	Succinate dehydrogenase (irreversible)

Menaquinone Dehydrogenases

Electron Donor	***Reactions***	***Reaction Names***
for_p	FDH5pp	Formate Dehydrogenase (menaquinone-8) (periplasm)
dhor__S_c	DHORD5	Dihydroorotic acid (menaquinone-8)
glyc3p_c	G3PD6	Glycerol-3-phosphate dehydrogenase (menaquinone-8)
glyclt_c	GLYCTO3	Glycolate oxidase
h2_c	HYD2pp	Hydrogenase (menaquinone8: 2 protons) (periplasm)
lac__L_c	L_LACD3	L-Lactate dehydrogenase (menaquinone)
mal__L_c	MDH3	Malate dehydrogenase (menaquinone 8 as acceptor)
nadh_c	NADH10	NADH dehydrogenase (menaquinone-8 & 0 protons)
nadh_c	NADH17pp	NADH dehydrogenase (menaquinone-8 & 3 protons) (periplasm)
nadph_c	NADPHQR3	NADPH Quinone Reductase (Menaquinone-8)

Demethylmenaquinone Dehydrogenases

Electron Donor	***Reactions***	***Reaction Names***
fum_c	FRD3	Fumarate reductase
glyc3p_c	G3PD7	Glycerol-3-phosphate dehydrogenase (demethylmenaquinone-8)
glyclt_c	GLYCTO4	Glycolate oxidase
h2_c	HYD3pp	Hydrogenase (Demethylmenaquinone-8: 2 protons) (periplasm)

nadh_c	NADH18pp	NADH dehydrogenase (demethylmenaquinone-8 & 3 protons) (periplasm)
nadh_c	NADH9	NADH dehydrogenase (demethylmenaquinone-8 & 0 protons)
nadph_c	NADPHQR4	NADPH Quinone Reductase (2-Demethylmenaquinone-8)

After the electrons have been transferred from the dehydrogenases to the quinones they are transferred to an oxidase or reductase and eventually to the terminal electron acceptors. The electron acceptors present in *E.coli* that are part of the cell's energy production include; oxygen (o2_c), nitrate (no3_c), dimethyl sulfoxide (dmso_c and dmso_p), Trimethylamine N-oxide (tmao_c and tmao_p). A table showing the relationship between the electron acceptors and the oxidases and reductases is shown below.

Ubiquinone Oxidases/Reductases

Electron Acceptor	***Reactions***	***Reaction Names***
asp__L_c	ASPO3	L-aspartate oxidase
o2_c	CYTBDpp	Cytochrome oxidase bd (ubiquinol-8: 2 protons) (periplasm)
o2_c	CYTBO3_4pp	Cytochrome oxidase bo3 (ubiquinol-8: 4 protons) (periplasm)
amet_c	DMQMT	3-Dimethylubiquinonol 3-methyltransferase
dsbard_p	DSBAO1	DsbA protein reoxidation reaction (aerobic)
no3_c	NO3R1bpp	Nitrate reductase (Ubiquinol-8)
no3_c	NO3R1pp	'Nitrate reductase (Ubiquinol-8) (periplasm)'
no2_p	NTRIR3pp	Nitrite Reductase (Ubiquinole-8, periplasm)
o2_c	QMO2	'Quinol monooxygenase (Ubiquinol-8)'

Menaquinone Oxidases/Reductases

Electron Acceptor	***Reactions***	***Reaction Names***
amet_c	AMMQLT8	S-adenosylmethione:2-demthylmenaquinole methyltransferase (menaquinone 8)
asp__L_c	ASPO4	L-aspartate oxidase
o2_c	CYTBD2pp	Cytochrome oxidase bd (menaquinol-8: 2 protons) (periplasm)
dmso_c	DMSOR1	Dimethyl sulfoxide reductase (Menaquinol 8)
dmso_p	DMSOR1pp	Dimethyl sulfoxide reductase (Menaquinol 8) (periplasm)
dsbard_p	DSBAO2	DsbA protein reoxidation reaction (anaerobic)
fum_c	FRD2	Fumarate reductase
no3_c	NO3R2bpp	Nitrate reductase (Menaquinol-8) (periplasm)
no3_c	NO3R2pp	Nitrate reductase (Menaquinol-8) (periplasm)
no2_c	NTRIR4pp	Nitrite Reductase (Menaquinole-8, periplasm)
o2_c	QMO3	Quinol monooxygenase (menaquinol 8)
sel_c	SELR	Selenate reductase
tmao_c	TMAOR1	Trimethylamine N-oxide reductase (menaquinol 8)
tmao_p	TMAOR1pp	Trimethylamine N-oxide reductase (menaquinol 8) (periplasm)

Demethylmenaquinone Oxidases/Reductases

Electron Acceptor	***Reactions***	***Reaction Names***
amet_c	AMMQLT8	S-adenosylmethione:2-demthylmenaquinole methyltransferase (menaquinone 8)
dhna_c	DHNAOT4	1,4-dihydroxy-2-naphthoate octaprenyltransferase
dmso_c	DMSOR2	Dimethyl sulfoxide reductase (Demethylmenaquinol 8)
dmso_p	DMSOR2pp	Dimethyl sulfoxide reductase (Demethylmenaquinol 8) (periplasm)
fum_c	FRD3	Fumarate reductase
tmao_c	TMAOR2	Trimethylamine N-oxide reductase (demethylmenaquinol 8)
tmao_p	TMAOR2pp	Trimethylamine N-oxide reductase (demethylmenaquinol 8) (periplasm)

Below are some diagrams that visually show the relationships between the electron donors, the dehydrogenases, the quinone pools and the oxidases and reductases for the electron transport chain of *E.coli*. The first is the ubiquinone pool. These figures begin on the left by showing all the dehydrogenases and their associated electron donor available for each quinone pool. On the right is a list of all the oxidases/reductases with their electron acceptors for a given quinone pool.

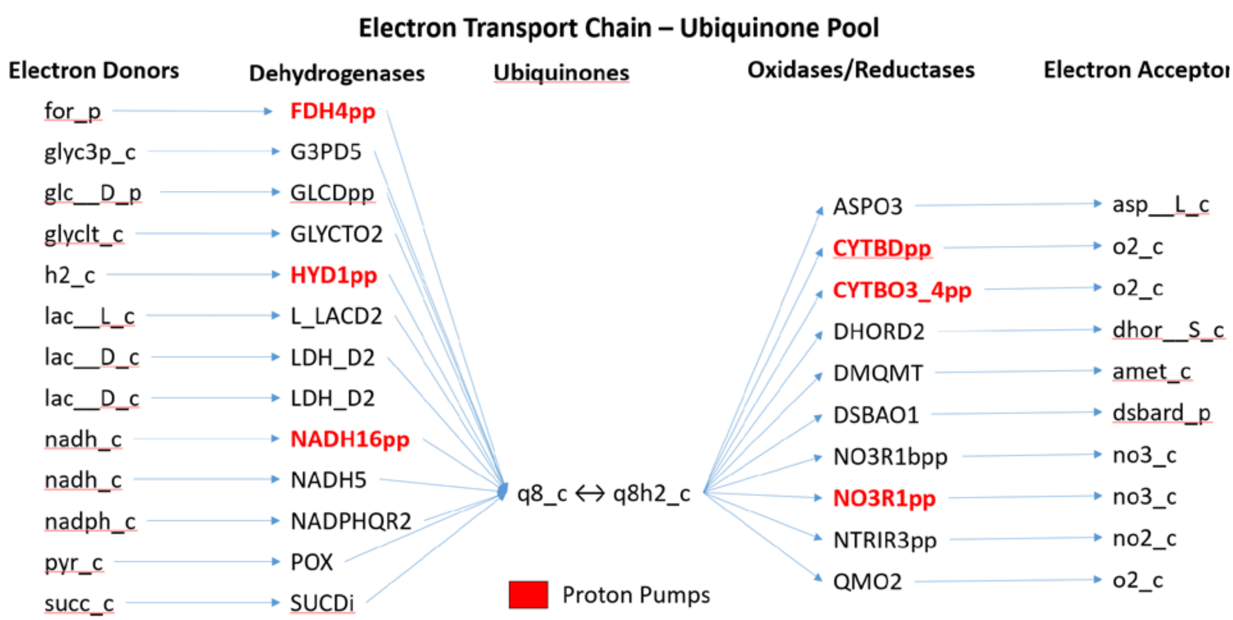

Figure 1. A diagram showing the relationships between the electron donors, the dehydrogenases, the ubiquinone pool and the oxidases and reductases for the electron transport chain of *E.coli*. The enzymes that also serve as proton pumps are shown in the red.

In Figure 1, the enzymes that also serve as proton pumps are shown in the red. Oxidative phosphorylation requires that protons are pumped from the cytoplasmic to the periplasmic space to create the proton-motive force that will force ATP synthase to produce atp_c. For the dehydrogenases there are three enzymes that can pump protons from the cytoplasmic to the periplasmic space. The enzyme NADH16pp is the primary dehydrogenase used in glucose-driven aerobic conditions. For this enzyme three protons are transferred to the periplasm for every two electrons that enter the enzyme. The other two dehydrogenases are only used in specific conditions; FDH4pp transfers one proton / two electrons while HYD1pp can transfer two protons / two electrons.

For the oxidases/reductases there are also three enzymes that are proton pumps: CYDBpp, CYTBO3_4pp, and NO3R1pp. For these enzymes CYDBpp and NO3R1pp transfers two protons / two electrons while CYTBO3_4pp transfers 4 protons /2 electrons.

For oxidative phosphorylation the P/O ratio (the ratio of protons pumped into the periplasmic space divided by the number of protons that re-enters the cytoplasmic space to create an atp_c) of these *E.coli* models can vary between an upper limit of 7/4 (NADH16pp & CYTBO3_4pp) and 3/4 (FDH4pp & CYDBpp). These ratios are different for both nitrate and fumarate respiration.

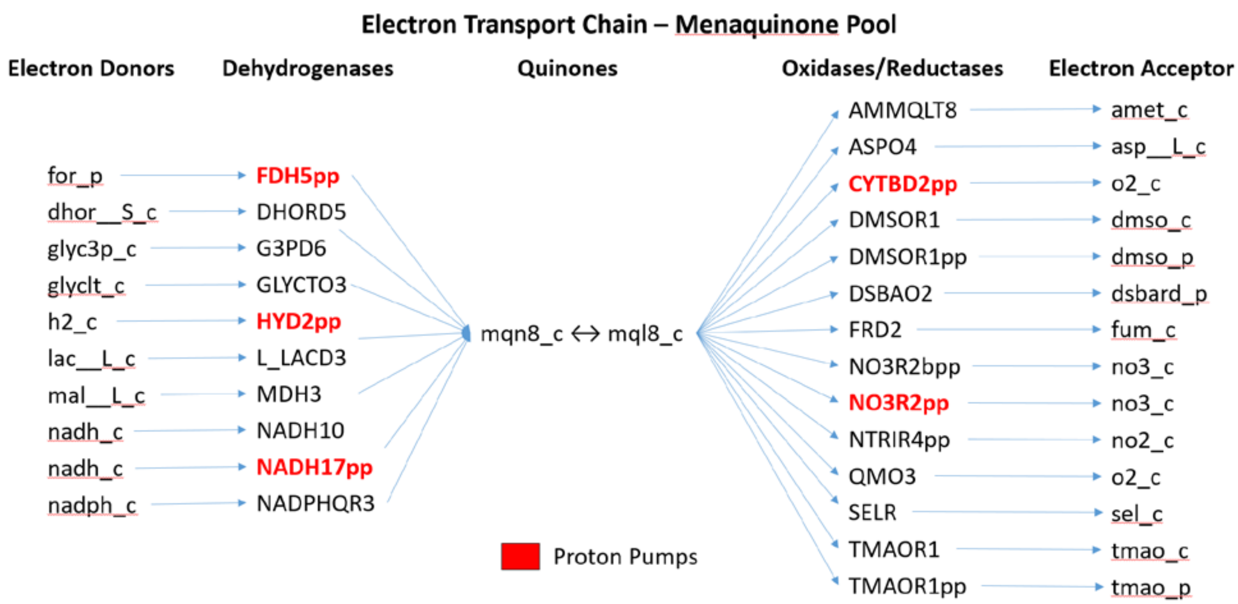

Figure 2. A diagram showing the relationships between the electron donors, the dehydrogenases, the menaquinone pool and the oxidases and reductases for the electron transport chain of *E.coli*. The enzymes that also serve as proton pumps are shown in the red.

In Figure 2, there are three dehydrogenases that can pump protons. The enzyme NADH17pp allows three protons to be transferred to the periplasm for every two electrons that enter the enzyme. The other two dehydrogenases are FDH5pp that can transfer one proton per two electrons while HYD2pp can transfer 2 protons / 2 electrons. For the oxidases/reductases there are also two enzymes that are proton pumps: CYTDB2pp and NO3R2pp which can both transfer 2 protons/ 2 electrons.

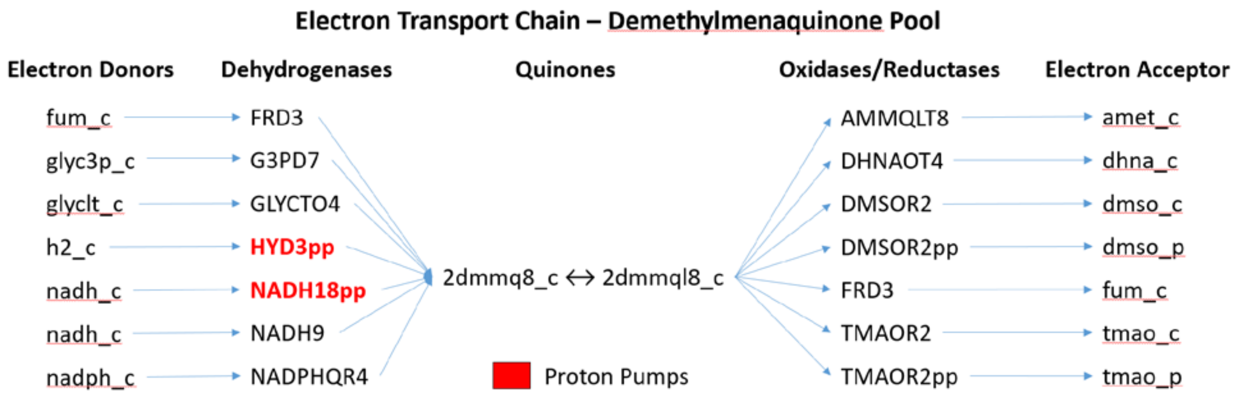

Figure 3. A diagram showing the relationships between the electron donors, the dehydrogenases, the demethylmenaquinone pool and the oxidases and reductases for the electron transport chain of *E.coli.* The enzymes that also serve as proton pumps are shown in the red.

In Figure 3, there are two dehydrogenases that can pump protons. The enzyme NADH18pp forces three protons to be transferred to the periplasm for every two electrons that enter the enzyme. The other dehydrogenase HYD3pp can transfer 2 protons / 2 electrons. For the oxidases/reductases there are no enzymes that are proton pumps.

[1]. D. White, “The physiology and biochemistry of prokaryotes,” Third edition, Oxford University Press, 2007.