Nitrogenase Electron Tunneling Pathways Analysis: From the 4Fe-4S Cluster to the P-cluster

by

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Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Department of
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ABSTRACT

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Abstract

The biological reduction of N₂ to NH₃ catalyzed by molybdenum nitrogenase requires eight steps to finish a completed catalysis cycle. This reaction cycle is associated with ATP-driven electron transfer (ET) from the Fe protein to the MoFe protein, and part of ET is experimentally confirmed to be ‘conformationally gated’. Although the overall sequence of ET in nitrogenase has been studied for decades, the nature of coupling between ET pathways and nucleotides binding/protein-protein docking is still unclear, especially from theoretical aspects. Here, we have utilized submicrosecond classical molecular dynamics simulations to allow the ADP-bound and ATP-bound nitrogenases to simulate their conformations in real biological systems. Then the Pathways plugin implemented by Balabin et al was employed to calculate the ET coupling and visualize the ET pathways between the F-cluster and the P-cluster in nitrogenase. The comparison of the ET couplings (the F-cluster to the P-cluster) we calculated and the edge-to-edge distance between the ET donor and acceptor suggests that the coupling pathways grow in strength more that that would be expected from simple distance changes. This result additionally indicates the electron of Fe protein is protected prior to the ATP binding and the protein-protein docking, using pathway switching effects.
# Contents

Abstract.................................................................................................................................................... iv

List of Tables.................................................................................................................................................. vii

List of Figures ............................................................................................................................................... viii

Acknowledgements ....................................................................................................................................... ix

1. Introduction ................................................................................................................................................ 1
   1.1 Nitrogen cycle on Earth ......................................................................................................................... 1
   1.2 Discovery of nitrogenase ......................................................................................................................... 2
   1.3 Nitrogenase structure ............................................................................................................................. 3

2. Nitrogen Fixation Reaction Mechanisms .............................................................................................. 6
   2.1 A working mechanism model of nitrogenase ......................................................................................... 6
   2.2 Deficit-spending model ......................................................................................................................... 9

3. Electron Tunneling Model and VMD Pathways Analysis plugin ............................................................ 12
   3.1 Electron tunneling model ...................................................................................................................... 12
   3.2 Tunneling pathways analysis ............................................................................................................... 13

4. Discovery of Insulated Electron ............................................................................................................. 14
   4.1 Molecular dynamics preparation ....................................................................................................... 14
      4.1.1 Model building .............................................................................................................................. 14
      4.1.2 Potential energy function setup .................................................................................................. 15
      4.1.3 Equilibration and restrained MD simulation .............................................................................. 16
   4.2 Pathways analysis with the Pathways plugin ...................................................................................... 19
5. Conclusion ............................................................................................................................................. 22

5.1 Percentage counting through the trajectory ......................................................................................... 22

5.2 Result and Discussion .......................................................................................................................... 24

References .................................................................................................................................................. 27
List of Tables

Table 1: Comparison of covalent bond numbers between the two protein complexes....23
List of Figures

Figure 1: A schematic representation of the bacterial nitrogen cycle[1] .........................1
Figure 2: the X-ray structure of ATP-bound molybdenum nitrogenase[2].....................4
Figure 3: Structures of cystine-bound cofactors[25] ..................................................5
Figure 4: the overall reaction working flow[25]................................................................7
Figure 5: a crude scheme for the relative positions of important cofactors for ADP-bound nitrogenase [33] .........................................................................................8
Figure 6: models for nitrogenase mechanism[38].........................................................10
Figure 7: implementation interface of Pathways plugin[43].............................................13
Figure 8: all-atom RMSD of ADP-bound nitrogenase (blue) and ATP-bound nitrogenase (red) .........................................................................................................................17
Figure 9: RMSD of residues on the ET pathways between the F-cluster to the P-cluster.18
Figure 10: parameters of ATP-bound nitrogenase MD simulation..............................18
Figure 11: parameters of ADP-bound nitrogenase MD simulation..............................19
Figure 12: overall view of important cofactors in nitrogenase ....................................20
Figure 13: pathways in ADP-bound nitrogenase that are 'indirect' ............................21
Figure 14: pathways in ATP-bound nitrogenase that are 'direct' ...............................21
Figure 15: overall scheme of effective covalent bond studies....................................24
Figure 16: coupled electron and insulated electron in nitrogenase.............................25
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1. Introduction

1.1 Nitrogen cycle on Earth

Nitrogen is widely distributed on Earth throughout hydrosphere, biosphere, atmosphere and lithosphere.[1, 2] The lithosphere contains ~94% of all nitrogen on Earth, ~6% in the atmosphere, and a small fraction (~0.006%) within the hydrosphere and biosphere. [1]

![Diagram of the nitrogen cycle](image)

**Figure 1: A schematic representation of the bacterial nitrogen cycle[1]**

As shown in figure 1, the nitrogen cycle is interconnected by multiple chemical transformations including dinitrogen fixation, denitrification (NO\(^3\) -> NO\(^2\)), nitrification (NH\(_2\)OH -> NO\(^3\)). Because fixed forms of N are continuously sequestered into sediments, rendering them unavailable for metabolism, and because they are also
continuously converted to $\text{N}_2$ through the combined processes of nitrification and denitrification, life can only be sustained by conversion of $\text{N}_2$ to $\text{NH}_3$.[1]

Nitrogen, especially when formed as ‘fixed nitrogen’ such as ammonia ($\text{NH}_3$) and nitrate ($\text{NO}_3^-$), is an element essential to support lives, which leads the nitrogen fixation reactions worthy of study.[3, 4] Nitrogen fixation reactions typically occur in three different ways: (i) some geochemical reactions initiated by lightning[5], (ii) biological processes catalyzed by nitrogenases[6, 7], (iii) manufactured industrially via Haber process.[8, 9] Nitrogenase existed two billion years ago, and catalyzed nitrogen fixation reactions since then.[10] Nowadays, nitrogen industrially fixed through the Haber-Bosch process takes around 45% among all the nitrogen fixed on Earth.[11] Knowing that more than half of the fixed nitrogen is produced through biological process, and the biological process catalyzes the nitrogen fixation reactions under room temperature and moderate pressure, it turns more important to understand the mechanism of nitrogenase catalyzed nitrogen fixation reactions.[2]

1.2 Discovery of nitrogenase

Scientist spent long time to study bio-catalyzed nitrogen fixation reactions.[2] In 1862, the first experimental evidence of nitrogen fixation by microorganisms was provided.[12] After near half of a century, the first nitrogen-fixing bacteria, *Azotobacter chroococcum*, was isolated and described in 1901 by Martinus Beijerinck, a Dutch microbiologist and botanist.[13] In 1934, Dr. Dean Burk in the Department of
Agriculture firstly named the metal-enzymes biologically catalyze the nitrogen fixation reactions as nitrogenase.[6, 14] With the help of development in the methods to extract nitrogenase from living bacteria, researchers conducted numerous efforts to uncover the structure nitrogenase.[15-18] The developments on the structure studies greatly helped the researches on nitrogen fixation mechanism[2], which will be introduced in the following chapter.

### 1.3 Nitrogenase structure

This kind of enzyme contains two component of protein subunits, called Fe protein and the MoFe protein.[19] There are several important cofactors in nitrogenases, including a 4Fe4S cluster, a P-Cluster and a FeMo-cofactor Cluster.[15, 20, 21]
As shown in the X-ray structure of molybdenum nitrogenase, there are two protein complexes in the molybdenum nitrogenase; the one containing of the 4Fe4S cluster, called F cluster, is called Fe protein. Meanwhile, the other protein complex called MoFe protein contains two metal cofactors, which are P cluster and M cluster. The space filing and stick models of 4Fe4S cluster (F cluster), P cluster and FeMo cofactor.

In the P-Cluster (Fe₇S₇), two [Fe₄S₃] cubes are linked by a sulfur central atom. This iron-sulfur cluster (P-Cluster) is involved in the electron transfer (ET) reaction from Fe protein to the FeMo cofactor.[21, 22] As the redox state of the P-cluster may change during the ET reaction, there exist forms of P-Cluster structure: one not bonded to Ser
beta - 188 and the other coordinated by the oxygen of deprotonated Ser Beta – 188.[23, 24]

Figure 3: Structures of cystine-bound cofactors[25]

The metal cofactors in the protein complexes are bound to several amino acid groups, such as cystine, histidine, and a homo-citrate cofactor. Especially, the structure of the P cluster including the cystines binding to it varies with its redox state. The net charge of the oxidized state of P cluster including 6 cystines is -3.[23, 25] As we will only analyze the electron transfer process between F cluster to P cluster, so the initial redox state of our molecular dynamics simulations are reduced F cluster and oxidized P cluster. Details of the net charge issue will be included in the last section. Like the F cluster and P cluster, the structure of MoFe-co also varies as its changing on its redox potential. It could be regarded as an electron pool, which is able to contain multiple electron. And
the intermediates during the reaction has been captured by Electron Paramagnetic Resonance (EPR) studies. [1, 19, 20, 22, 23, 26-29]

2. Nitrogen Fixation Reaction Mechanisms

Although it is well known that nitrogenases catalyze the nitrogen fixation reactions, there are existing debates regarding on two questions. 1) the sequence of working model for a cycle of ATP hydrolysis-coupled electron transfer in molybdenum nitrogenase 2) structures of MoFe-co intermediates \( E_n \), \( n = 0 - 8 \) corresponding to the number of electron transfer.[2, 25, 30-32]

2.1 A working mechanism model of nitrogenase

As we discussed before, a molybdenum nitrogenase consists of two proteins. The one, containing the 4Fe-4S cluster and bound with two ADP/ATP complexes, is called Fe protein. Other metal clusters (P cluster and FeMo-co) are located in the other protein called MoFe protein. Compared with MoFe protein (about 240 kD), Fe protein is smaller (about 60 kD).[25] The overall nitrogen fixation reaction catalyzed by nitrogenase is

\[
N_2 + 8H^+ + 8e^- + 16MgATP \rightarrow 2NH_3 + H_2 + 16MgADP + 16Pi
\]

To uncover a detailed mechanism of nitrogenase, several experimental and theoretical groups conducted researches. Let us delve into the discovery and the development of nitrogenase mechanism studies.

In 2000, researchers at Catech and University of Minnesota proposed a possible mechanism for the electron transfer process in nitrogenase. According to their result,
two protein complexes (Fe protein and MoFe protein) is bound prior to the ET reactions between the metal cofactor in the two protein complexes. At that time, the 4Fe-4S cluster is in the reduced state, and the Fe protein is bound to two ATP complexes. They suggested the P cluster plays a critical role in the ET between Fe protein and the MoFe protein. After the ET reaction finishes, a dissociation of the Fe protein and the MoFe protein occurs, accompanied by the exchange of ADP to ATP and the 4Fe-4S cluster oxidization. [33] In 2003, Kurnikov and co-workers summarized this working flow based on the existing experimental data then.[25]

![Figure 4: the overall reaction working flow](image)

This working model to some extension was consistent to several experimental observations. For example, as shown in figure 5, the P cluster is located in the middle of...
the Fe protein and the MoFe protein, which is consistent with the claim that the electron transfer ‘proceeds through’ the P cluster.[33, 34] Second, the edge-to-edge distance between the 4Fe-4S cluster and the MoFe-co is approximately 14 Å, and this distance is compatible with the fact that ‘inter-protein electron transfer rates is more rapid than the observed turnover time’. [33, 35, 36]

Figure 5: a crude scheme for the relative positions of important cofactors for ADP-bound nitrogenase [33]
The formation of the bound protein complex is suggested to be followed by the electron transfer between Fe protein and MoFe protein. Although a crude picture of nitrogenase catalyzed nitrogen fixation reaction is drawn, the role and behavior of important cofactors of the nitrogen fixing reaction is still unknown, such as the relationship between ATP hydrolysis and ET in the protein complex, and especially, when and how all the cofactors interact as the electron transfer between the Fe protein and MoFe protein. All of these questions are waiting to be uncovered by reasonable mechanisms, as well as sufficient supporting experimental data, until the deficit-spending model of nitrogenase fixing reactions is proposed.

### 2.2 Deficit-spending model

Danyal and co-workers in 2010 experimentally showed that the electron transfer between the Fe protein and the MoFe protein is ‘gated’ by conformational changes of the molybdenum nitrogenase complex.[37] Additionally, crystal structures of ADP-bound and ATP-bound nitrogenases suggest that ATP hydrolysis is the reason for the conformational changes. That is to say, the intercomponent ET is ‘gated’ by the ATP hydrolysis, although the detailed sequence of intercomponent ET was still unknown for them.[37]

Danyal and co-workers in 2011 reported the evidence for the deficit-spending mechanism, which initiated a model for the mechanism.[38] With the help of stopped-flow kinetic measurement of ET from the Fe protein to the MoFe protein of the
molybdenum nitrogenase protein complex, they determined that the rate constant from the F cluster to the P cluster is 1700 s\(^{-1}\), while the observed overall rate constant from the Fe protein to the MoFe protein is 168 s\(^{-1}\). So, it can be concluded that this evidence supported the deficit-spending model, in which electron at first transports from the P cluster to the MoFe cofactor, and then follows by the ET from the F cluster to the P cluster, whose ET rate is much slower.[38]

**Figure 6: models for nitrogenase mechanism**[38]

They also studied the role of nucleotide (ATP, ADP + Pi, and AMPPCP) in nitrogenase complex. According to their study, neither of the ATP analogues, including ADP-AlF4, AMPPCP, supported the ET from P-cluster to the MoFe cofactor. However, the backfill electron transfer event (F cluster to P cluster) is supported by all kinds of
nucleotide binding. So it can be concluded that the ET from F-cluster to the P-cluster is not conformational gated, while the ET from P-cluster to the MoFe-co is conformational gated. Based on their results, a working model for nitrogenase mechanism of nitrogen fixation reactions can be draw as Figure 6.[38]
3. Electron Tunneling Model and VMD Pathways Analysis plugin

To study the electron transfer events in the nitrogenase, we employed a VMD plugin, which uses electron tunneling model, to calculate the ET coupling. In this chapter, the electron tunneling model and the VMD pathways analysis plugin will be briefly introduced.

3.1 Electron tunneling model

Biological ET reaction rates are known to approximately decrease over tunneling distance, exponentially.[39, 40] Meanwhile, water may mediate the electron tunneling while water presents higher barriers than protein, the exponential decay factors from different proteins are different. In the Pathways model, tunneling propagation is treated as a sequence of tunneling steps.[41] There are three types of mediated step based on Pathways model: a covalent bond, a hydrogen bond and a through vacuum space jump in Å.[41] The exponential decay factors for different mediates are different, and the electronic coupling is proportional to a product of penalties for each mediated step.[41]

Meanwhile, ε^C is assigned as 0.6 based on semi-empirical data.[42] The penalty for a vacuum through space mediated step is ε^S = ε^C exp[ −β^S(R^S − 1.4)]. Here R^S is distance of through space jump. Additionally, the penalty for the through hydrogen-bond-mediated step is ε^H = (ε^C)^2 exp[ −β^S(R^H − 2.8)]. Here the decay factor β^S is assigned as 1.1 Å⁻¹ based on typical co-factor binding energies.
3.2 Tunneling pathways analysis

In this subsection, the interface of the Pathways plugin will be briefly introduced. As shown in Figure 7, this plugin firstly loads the atoms’ coordinates and structures (adjacency information) from the PDB/DCD and PSF files. Then the binary executable file ‘pathcore’ basically employs Dijkstra’s algorithm to search the shortest path in the modeled graph. There are three different weights in the undirected graph, corresponding to three different mediated step according to the Pathways model.[41, 43] Details of the implementation interface can be found in Balabin’s article.[43]

![Diagram of the implementation interface of Pathways plugin](image)

Figure 7: implementation interface of Pathways plugin[43]
4. Discovery of Insulated Electron

According to the deficit-spending model for nitrogenase catalyzed reactions, the $P^N \rightarrow M^N$ ET step initiates the sequential ET when hydrolysable ATP nucleotides bind to the Fe protein.\[44\] After a single ET completes, two ATP complexes hydrolyze, and then the Fe protein and the MoFe protein disassociate. In the whole process, the backfill ET ($F^{1+} \rightarrow P^{1+}$) requires the ATP nucleotides binding, although it doesn’t require a hydrolysable ATP.\[38, 44\]

According to the original crystal structures of ADP-bound nitrogenase and the ATP-analogue-bound nitrogenase (AMPPCP-bound nitrogenase), the edge-to-edge distance between the F-cluster and the P-cluster in the ATP-bound nitrogenase is $X$ Å and that in the ADP-bound nitrogenase is $X$ Å.\[45\] Consequently, we may ask a question: if the difference in distance is the only reason for the stronger ET coupling in ATP-bound nitrogenase? To answer this question, we simulated the nitrogenase ET in water-solvated environment over 150-ns time scale. Additionally, the Pathways plugin discussed in the previous chapter was employed to calculate the ET coupling between the F-cluster and the P-cluster.

4.1 Molecular dynamics preparation

4.1.1 Model building

The starting geometry of the nitrogenases were taken from X-ray structure of ADP and ATP-bound molybdenum nitrogenase from Azotobacter vinelandii (Protein
Data Bank ID 2AFI and 4WZB).[45] To save time for molecular simulation, the tetramer is truncated to a monomer. The protonation state of the histidines was determined by PropKa.[46] After the pH environment was set to 7 (to simulate the real biology environment) and the histidines protonation state was determined, two monomer nitrogenases were inserted into rectangular water boxes. The water box for ATP-bound structure is $140 \times 140 \times 140 \, \text{Å}^3$, whose total atom number for simulation is 250 000. Meanwhile, the water box for ADP-bound structure is $140 \times 140 \times 140 \, \text{Å}^3$, and the total number of it is 200 000.

### 4.1.2 Potential energy function setup

A set of well-prepared potential energy terms for each atom is crucial for molecular dynamics simulations. We selected TIP3P model to describe water molecules.[47] For the protein, CHARMM27 force field parameters were chosen for simulation.[48] The force field parameters of the F-cluster was taken from the supporting information from Chang et al’s article in 2009.[49] Meanwhile, we took the force field parameters of the P-cluster and the MoFe cofactor from Smith et. al’s article published in 2014.[50] Same as their treatment to metal clusters, the equilibrium bond lengths and angles were taken directly from their original crystal structures.[45] Stiff bond and angle constants of them were assigned large enough to maintain their initial configuration. ($k_r = 500 \, \text{kcal mol}^{-1} \, \text{Å}^2$, $k_a = 200 \, \text{kcal mol}^{-1} \, \text{rad}^2$) The non-integer net charge for those cofactors were normalized to the redox-state they should be. The force field
parameters of other non-metal cofactors, including AMPPCP, ADP and HCA (homocitrate), were parameterized by an online toolkit, SwissParam.[51] Nickel and iron’s Lennard-Jones parameters were taken from Smith et al.[52] The L-J parameters of Mo were copied from Ni.[50]

4.1.3 Equilibration and restrained MD simulation

All classical MD simulations were conducted with NAMD 2.1 program.[53] The solvated structures were minimized by energy to a maximum atomic force tolerance of 12 kcal mol$^{-1}$ Å$^{-1}$. Then the energy minimization structures were used as the starting structures of restrained equilibration. All the MD simulations in this project were under 300 K and the pressure was maintained at 1 atm. After the energy minimization, all the water molecules were realized to fully-equilibrated. Then the water molecules were frozen, the protein was gradually released, with constraint atom force tolerance gradually decreasing from 99 kcal mol$^{-1}$ Å$^{-1}$ to 0 kcal mol$^{-1}$ Å$^{-1}$. After the restrained equilibration, the protein together with all water molecules were released before running the production run. Here is the all atom root-mean-squared deviation (RMSD) with the first frame of the production run as reference page.
According to the figure above, the range of the RMSD for the two protein complexes is ~3.5 Å. This value is large enough for an equilibrated system. However, considering the original structure of the molybdenum nitrogenase (both ADP-bound and ATP-bound nitrogenases), Van-der-Waals constraints did exist in the dimer. After the dimer was truncated to two monomers, the constraints vanished. Considering the root-mean-squared fluctuation (RMSF) of residues, the mostly fluctuated residues are all on the surface of the monomer. Then I examined the RMSD of important residues that are on the electronic tunneling pathways between F-cluster and the P-cluster.
Figure 9: RMSD of residues on the ET pathways between the F-cluster to the P-cluster

Observing from Figure 9, the range of import residues’ RMSD for the two protein complexes is ~1.3 Å, meaning that the important residues were equilibrated during the production run of MD simulation. Besides, other parameters, including temperature, VDW forces, pressure, and the volume of the water box, were also examined. The results of these parameters can be seen in Figure 10 and Figure 11.

Figure 10: parameters of ATP-bound nitrogenase MD simulation
According to the parameters over the MD trajectory and the RMSD of important residues of the two protein complexes (ADP-bound and ATP-bound nitrogenases), the trajectory of the production run is completely equilibrated, and the following analysis based on these trajectories is reliable.

4.2 Pathways analysis with the Pathways plugin

To simulate the catalysis process in real biological environment, which is solvated by water molecules, under 1 atm pressure and 300 K. Then the edge-to-edge distances between the F-cluster and the P-cluster in the two protein complexes (ADP-bound and ATP-bound nitrogenases) were measured. As shown in Figure 12, the difference of distances is ~1.8 Å. And then, the pathways analysis of pathways between the ET donor (F-cluster) to the ET acceptor (P-cluster) was conducted.
We simulated ~150 ns for the two protein complexes. All the distances shown in Figure 12 are the average distances over trajectories. Then we come back to the original question: is the difference in distance the only reason for the stronger ET coupling between the F-cluster and the P-cluster in the ATP-bound than that in the ADP-bound nitrogenase?

As shown in the Figure 13, different ET pathways of ADP-bound nitrogenase over the trajectory is visualized. The pink cubic residue on the left hand side is the F-cluster of the ADP-bound nitrogenase, and the silver residue on the right hand side is the P-cluster, which is the ET acceptor. There are three major kinds of ET pathways in the ADP-bound nitrogenase. (A) Route: SF4 1290, CYS 97, LEU 158, CYS 154, CLF 3498. This kind of route takes 62.74% of all ET pathways. (B) Route: SF4 1290, CYS 97, ILE 158, MET 154, CYS 153, CLF 3498. This kind of route takes 10.53% of all ET pathways. (C)
Route: SF4 1290, LEU 158, CYS 154, CLF 3498. This kind of route takes 8.85% of all ET pathways.

Figure 13: pathways in ADP-bound nitrogenase that are 'indirect'

As shown in Figure 14, there are two dominant ET pathways in the ATP-bound nitrogenase. (A) Route: SF4 3290, CYS 97, ILE 159, PRO 155, CYS 154, CLF 3498. This kind of route takes 44.60% of all ET pathways. (B) Route: SF4 3290, CYS 97, ARG 100, PHE 186, CYS 154, CLF 3498. This kind of route takes 33.53% of all ET pathways in the ATP-bound nitrogenase's trajectory.

Figure 14: pathways in ATP-bound nitrogenase that are 'direct'

Visually comparing the ET pathways in the ATP-bound nitrogenase with those in the ADP-bound nitrogenase, the ET pathways in the ATP-bound nitrogenase can be seen more direct. According to the Pathways model, more ET steps in the pathway
corresponds to a weaker coupling if mediated by same mediations (hydrogen bonds, vacuum, covalent bonds).[41] Although more supporting information is required (will be discussed in the next subsection), the more direct ET pathways suggest that coupling pathways may grow in strength on ATP binding more than that would be expected from simple distance changes. To validate this assumption, we turned the ET coupling to the difference of effective covalent bond numbers and conducted further analysis.

5. Conclusion

5.1 Percentage counting through the trajectory

In the Pathways models, the penalty for a through covalent bond ET jump is 0.6.[42] So we can introduce a coupling metric the effective covalent bond number, to describe strength of ET coupling. For the two protein complexes, we have: $H_{\text{DA(ADP)}} = A_{\text{ADP}} 0.6 N_{\text{ADP}}$, and $H_{\text{DA(ATP)}} = A_{\text{ATP}} 0.6 N_{\text{ATP}}$. $H_{\text{DA}}$ is the ET coupling; $A_{\text{ADP}}$ and $A_{\text{ATP}}$ are the pre-factors mentioned in the Pathways model.[41] Now we can make an assumption that the two pre-factors are equal. This assumption is reasonable because the pre-factor depends on the structure of the ET donor and acceptor. Although the configurations of the two protein complexes for simulation are different, the redox-state and the structure of the ET donor and acceptor are same. So, the pre-factors for the two structures can be assumed to be equal. Then the difference of the covalent bond numbers between the two protein complexes can be calculated.
To answer the question raised in the previous section, we also turned the edge-to-edge distance between 4Fe-4S cluster and the P-cluster to the number of covalent bonds. The difference of edge-to-edge distance in terms of covalent bond numbers between the two protein complexes can be calculated by: $\Delta N = (R_{ADP} - R_{ATP}) / 1.4 \, \text{Å}$. Here the length of a covalent bond is assigned as 1.4 Å, and $R_{ADP}$ and $R_{ATP}$ represent the edge-to-edge distance between the F-cluster and the P-cluster.

By comparing the difference between $\Delta N_{\text{effective}}$ and $\Delta N_{\text{edge-to-edge}}$, the question raised previously can be uncovered. Because the configurations of different pathways may influence the coupling as well as the effective covalent bond numbers, we examined $\Delta N$ for different ET pathway types.

Table 1: Comparison of covalent bond numbers between the two protein complexes

<table>
<thead>
<tr>
<th>Covalent bond number differences</th>
<th>ATP – 1 (63%)</th>
<th>ATP – 2 (11%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pathway</td>
<td>physical</td>
</tr>
<tr>
<td>ADP – 1 (44.6%)</td>
<td>3.9</td>
<td>1.6</td>
</tr>
<tr>
<td>ADP – 2 (33.4%)</td>
<td>3.9</td>
<td>1.1</td>
</tr>
</tbody>
</table>

As shown in Table 1, the effective covalent bond number differences of ET pathways were represented as ‘pathway’, and the covalent bond number differences of edge-to-edge physical distance were represented as ‘physical’ in the table. The percentage fractions of different ET pathways were labeled along the nitrogenase name.
According to Table 1, the ET coupling differences in terms of covalent bond numbers are much larger than the edge-to-edge distance differences between the ADP-bound nitrogenase and the ATP-bound nitrogenase. This results strongly supported the assumption we made, that is: coupling pathways grow in strength on ATP binding/docking more than that would be expected from simple distance changes.

Then we again examined the average differences without considering different pathways types. The ET coupling between F-cluster and the P-cluster grows 4.0 covalent bonds while the edge-to-edge distance only grows 1.3 covalent bonds.

**Figure 15: overall scheme of effective covalent bond studies**

### 5.2 Result and Discussion

Recalling the mechanism of nitrogen fixing reaction catalyzed by nitrogenase, especially the deficit-spending model, ET step (P-cluster to MoFe-co) is followed by the ET (F-cluster to P-cluster) when Fe protein and the Mo protein are associated. One point to highlight: the backfill ET step requires the ATP/ATP-analouges binding but doesn’t require a hydrolysable ATP binding. Besides, the protein-protein dissociation occurs
after ET finishes and the ATP hydrolysis. Because our simulation results suggest that coupling pathways grow in strength on ATP binding/docking more than that would be expected from simple distance changes, we can conclude there should exist some critical structural reasons that make the ET pathways more indirect in the ADP-bound nitrogenase.

These indirect pathways weakened the ET coupling compared with the ATP-bound nitrogenase. So, the ADP binding Fe protein protected its electron prior to ATP binding and the protein-protein docking using pathways switching effects.

Figure 16: coupled electron and insulated electron in nitrogenase
As shown in Figure 16 (figure was partially taken from Duval et al’s paper[44]), the electron in the F-cluster is insulated/protected by ADP binding, till the ATP binds to the Fe protein and the Fe protein/MoFe protein associates again for the next ET cycle.
References


