

# The Roots of Modern Biochemistry

Fritz Lipmann's Squiggle  
and its Consequences

Editors

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# Bioenergetics of Protein Transport into Mitochondria: Role of $\Delta\Psi$ and of Nucleoside Triphosphates

*Nikolaus Pfanner and Walter Neupert*

## Introduction

The majority of mitochondrial proteins are encoded by nuclear genes. They are synthesized on cytosolic polysomes as soluble precursor proteins and are then transported into one of the four mitochondrial compartments (outer membrane, intermembrane space, inner membrane, and matrix) (for review see Ref. 1). Many precursors contain amino-terminal peptide extensions (presequences) which apparently carry information for the targeting to mitochondria (for review see Ref. 2). Recent studies, however, show that non-aminoterminal precursor regions can also contain information for specific import into mitochondria (3, 4). The precursor proteins bind to receptor sites on the mitochondrial surface (5–7) and are then translocated into or across the mitochondrial membranes. Many precursors are imported at sites of close contact between outer and inner mitochondrial membranes (contact sites) (7–11). The presequences are proteolytically processed by a processing peptidase located in the mitochondrial matrix (12, 13). Some precursors, which are destined for the intermembrane space or the outer face of the inner membrane, are first completely imported into the matrix and are then retranslocated across the inner membrane ('conservative sorting') (9, 14). Many precursors are assembled into multi-subunit complexes (9, 15).

Several steps on the import pathways of mitochondrial precursor proteins require energy, either in the form of nucleoside triphosphates (NTPs) or in the form of the membrane potential ( $\Delta\Psi$ ) across the inner mitochondrial membrane. NTPs and  $\Delta\Psi$  are necessary for different stages in the protein import pathways.

## General Aspects of Energy Requirement of Protein Import

In very early studies on the biogenesis of mitochondrial proteins it was shown that energy was required for import of proteins into mitochondria. Uncouplers of oxidative phosphorylation (protonophores) prevented transport of proteins into mitochondria both *in vivo* and *in vitro* (16–18). Protonophores dissipate the electrochemical potential across the inner mitochondrial membrane. This subsequently leads to a decrease of the level of ATP. Hence, from these studies it could not be decided which form of energy (ATP or the electrochemical potential or both) was necessary for the protein import.

## Role of the Membrane Potential

Schleyer et al. (19) generated conditions where the electrochemical potential across the inner membrane was abolished whereas the levels of ATP inside and outside the mitochondria were high. This involved the use of protonophores (CCCP and FCCP),  $K^+$  ionophores (valinomycin), inhibitors of the electron transport chain (rotenone, antimycin A, and potassium cyanide), inhibitors of the  $F_0F_1$ -ATPase (oligomycin) and of the ADP/ATP translocator (ADP/ATP carrier) of the inner membrane (carboxyatractyloside). The transport of precursor proteins, which were synthesized *in vitro* in rabbit reticulocyte lysates, into isolated mitochondria was then investigated. Only when the inner membrane was energized, could precursor proteins be transported into or across the inner membrane. Similar results were obtained by Gasser et al. (20) and Kolanski et al. (21).

Some precursor proteins are not translocated across the inner membrane. These include proteins of the outer membrane and the intermembrane space protein cytochrome *c*. The import of these proteins does not require an electrochemical potential (18, 22–24). Other proteins of the intermembrane space (e. g., cytochrome *c* peroxidase and cytochrome  $b_2$ ) are first transported across the inner membrane and are then retranslocated to the intermembrane space (25, 26). Thus, their import needs the electrochemical potential across the inner membrane.

To understand the role of the electrochemical potential in protein import it was important to know which components of the total protonmotive force, i.e. the electrical component  $\Delta\Psi$  or the chemical component  $\Delta\text{pH}$  or both, were required. For this purpose, the electron transport chain and the  $F_0F_1$ -ATPase were inhibited and a valinomycin-induced potassium diffusion potential was generated. The translocation of the precursor of the ADP/ATP carrier from the outer into the inner membrane could be driven by this  $K^+$  diffusion potential. This import could not be abolished by protonophores and imposing a  $\Delta\text{pH}$  did not stimulate this import. Thus, a movement of protons across the inner membrane (driven by the total protonmotive force or by the  $\Delta\text{pH}$ ) was not required for protein import. We concluded that the electrical potential  $\Delta\Psi$  per se was the necessary energy source for protein transport into the inner membrane (27). It was calculated that relatively low potentials (20–40 mV) were able to drive import. It should be emphasized that the generation of translocation intermediates was a prerequisite for studies using a  $K^+$  diffusion potential and for several of the studies on the role of NTPs (see below). The protein import pathways could be divided into several subsequent steps and precursor proteins were reversibly accumulated on distinct stages of their import pathway (7, 8, 27, 28). This permitted studying defined steps of the protein import. The overall import *in vitro* of the ADP/ATP carrier from the cytosol into the inner membrane was too slow to be driven by a  $K^+$  diffusion potential: the diffusion potential was degraded before the binding of precursor to the mitochondrial surface had occurred. The translocation of precursor from the outer to the inner membrane, however, was rapid (less than 1 min) and therefore could be driven by the  $K^+$  diffusion potential (27).

Only the initial entrance of precursor proteins into the inner membrane required  $\Delta\Psi$ , the completion of translocation into or across the inner membrane was

observed to occur also in the absence of  $\Delta\Psi$  (7, 8). In the cases of precursor proteins which are synthesized as larger precursors, the positively charged amino-terminal presequences are involved in their entrance into the inner membrane.

In summary, we suggest that the role of the membrane potential  $\Delta\Psi$  in mitochondrial protein import involves an electrophoretic effect on the positively charged presequences (or positively charged regions in precursors without cleavable peptide extensions). Thereby  $\Delta\Psi$  triggers the initial entrance of the precursor into the inner membrane.

## Role of Nucleoside Triphosphates (NTPs)

The *in vitro* import system, rabbit reticulocyte lysates and isolated mitochondria, was depleted of ATP and ADP by pre-incubation with apyrase (an ATPase and an ADPase). A mitochondrial membrane potential was then established by addition of substrates of the electron transport chain and the  $F_0F_1$ -ATPase was inhibited to prevent dissipation of  $\Delta\Psi$  and synthesis of ATP. Under these conditions, the import of the precursor of  $F_0F_1$ -ATPase subunit  $\beta$  ( $F_1\beta$ ) was inhibited. Re-addition of ATP or GTP, but not of non-hydrolyzable ATP-analogues, restored the import (29). We concluded that both  $\Delta\Psi$  and NTPs were required for transport of  $F_1\beta$  into mitochondria. Similar results were obtained by studies using a purified precursor protein (30) or desalted reticulocyte lysate (31).

A requirement for NTPs has now been demonstrated for the import of a number of precursor proteins, including that of porin (an outer membrane protein) (32), cytochrome  $b_2$  (an intermembrane space protein) (33), ADP/ATP carrier and cytochrome  $c_1$  (inner membrane proteins) (33, 34),  $F_1\beta$  (inner face of the inner membrane) (29, 31, 34), and of chimaeric proteins consisting of (parts of) mitochondrial precursors and non-mitochondrial passenger proteins (30, 34, 35). It is especially interesting that the import of porin into the outer membrane, which is independent of  $\Delta\Psi$ , requires NTPs.

NTPs were required both for the initial interaction of precursor proteins with mitochondria and for the completion of transport of precursor proteins from the mitochondrial surface into mitochondria. The latter reaction required higher levels of NTPs than the former initial interaction. The precursor of  $F_0F_1$ -ATPase subunit 9 and a fusion protein consisting of the entire subunit 9 precursor and cytosolic dihydrofolate reductase required very different levels of NTPs for import into mitochondria. The requirement for NTPs did therefore not seem to be correlated to a specific step occurring at the mitochondrial membranes (like e.g. binding of precursor to receptor sites). We concluded that NTPs were necessary to confer import-competence to the precursor proteins (34). NTPs may act in concert with a recently proposed defolding enzyme ('unfoldase') (36) to keep mitochondrial precursor proteins in an import-competent conformation. This view is supported by the following two observations. 1. Whereas the import of *in vitro* synthesized porin required NTPs (32; see above), was the import of a denaturated ('defolded') form of the porin precursor independent of NTPs. The other import properties such as binding to a specific receptor protein were identical for both forms of the porin

precursor. Thus, the differential requirement for NTPs seems to be caused by different conformations of the precursors (Pfanner, Pfaller, Kleene and Neupert, in preparation). 2. The import of incompletely synthesized precursor chains into mitochondria required lower levels of NTPs than the import of the corresponding completed precursor proteins (35). On the assumption that incompletely synthesized chains are more loosely folded than completed chains, this result again supports the model that NTPs are involved in modulating the folding state of precursor proteins.

It is not known if the proposed defolding enzyme is located in the cytosol or is associated with the mitochondrial membranes. Furthermore, since the import system used contains nucleoside phosphate kinases, it has not been possible so far to decide which form of NTP, e.g. ATP or GTP, is directly required.

## Energy Requirement of Protein Translocation across Other Biological Membranes.

The translocation of proteins into chloroplasts (37–39) and across the membrane of the endoplasmic reticulum (ER) (40–44) were shown to require ATP. Wiech et al. (45) proposed that the ATP requirement for protein transport into the ER was related to the preservation of transport competence of the precursor protein. So far, a requirement for an electrochemical potential could not be demonstrated with chloroplasts and the ER. The export of proteins in *Escherichia coli* requires both the electrochemical potential across the plasma membrane and ATP (46, 47).

In summary, it appears that the energy requirements for translocation of proteins across different biological membranes are similar in several aspects. It remains unclear if the inability to show a requirement for an electrochemical potential in the cases of chloroplasts and the ER is caused by membrane-specific properties or by experimental conditions.

## Perspectives

The molecular details of the action of NTPs and of the membrane potential in mitochondrial protein import are still unknown (as is the case for protein transport across other biological membranes). Purification and characterization of the participating components are an important step to an understanding of these processes. This includes – besides the precursor proteins themselves – the proposed defolding enzyme(s) and components in the mitochondrial membranes (e.g., in contact sites) which mediate the protein translocation into the inner membrane.

The interaction of chemically synthesized mitochondrial presequences with artificial lipid membranes has been shown to depend on a transmembrane electrical potential (48). However, the significance of this biophysical model system for mitochondrial protein import remains unclear, since protein import into mitochondria has been shown to occur through a hydrophilic (probably proteinaceous) membrane environment (7, 10). Thus, the *in vitro* reconstitution of all participating components will be necessary to understand mitochondrial protein import at the molecular level.

An undeveloped field which might attract much interest in the near future is the energy requirement for protein transport out of the mitochondrial matrix into or across the inner membrane. This protein export includes mitochondrially synthesized precursor proteins and also cytoplasmically synthesized precursor proteins which are first imported into the matrix and are then retranslocated across the inner membrane (9, 14). This protein translocation into or across the inner mitochondrial membrane could occur in analogy to protein export in prokaryotes.

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## References

1. Pfanner, N. and Neupert, W. 1987. *Curr. Top. Bioenerg.* 15, 177–219.
2. Hurt, E. C. and van Loon, A. P. G. M. 1986. *Trends Biochem. Sci.* 11, 204–207.
3. Pfanner, N., Hoeben, P., Tropschug, M. and Neupert, W. 1987. *J. Biol. Chem.* 262, 14851–14854.
4. Pfanner, N., Müller, H. K., Harmey, M. A., and Neupert, W. 1987. *EMBO J.* 6, 3449–3454.
5. Zwizinski, C., Schleyer, M., and Neupert, W. 1984. *J. Biol. Chem.* 259, 7850–7856.
6. Pfaller, R. and Neupert, W. 1987. *EMBO J.* 6, 2635–2642.
7. Pfanner, N. and Neupert, W. 1987. *J. Biol. Chem.* 262, 7528–7536.
8. Schleyer, M. and Neupert, W. 1985. *Cell* 43, 339–350.
9. Hartl, F.-U., Schmidt, B., Wachter, E., Weiss, H. and Neupert, W. 1986. *Cell* 47, 939–951.
10. Pfanner, N., Hartl, F.-U., Guiard, B. and Neupert, W. 1987. *Eur. J. Biochem.*, 169, 289–293.
11. Schwaiger, M., Herzog, V. and Neupert, W. 1987. *J. Cell Biol.* 105, 235–246.
12. Böhni, P., Gasser, S., Leaver, C. and Schatz, G. 1980. In: *The Organization and Expression of the Mitochondrial Genome* (Kroon, A. M. and Saccone, C., eds.) pp. 423–433, Elsevier/North-Holland, Amsterdam.
13. Schmidt, B., Wachter, E., Sebald, W. and Neupert, W. 1984. *Eur. J. Biochem.* 144, 581–588.
14. Hartl, F.-U., Pfanner, N. and Neupert, W. 1987. *Biochem. Soc. Trans.* 15, 95–97.
15. Schmidt, B., Hennig, B., Zimmermann, R. and Neupert, W. 1983. *J. Cell Biol.* 96, 248–255.
16. Hallermayer, G. and Neupert, W. 1976. In: *Genetics and Biogenesis of Chloroplasts and Mitochondria* (Bücher, Th., Neupert, W., Sebald, W. and Werner, S., eds.), pp. 807–812, North-Holland, Amsterdam.
17. Nelson, N. and Schatz, G. 1979. *Proc. Natl. Acad. Sci. USA* 76, 4365–4369.
18. Zimmermann, R., Hennig, B. and Neupert, W. 1981. *Eur. J. Biochem.* 116, 455–460.
19. Schleyer, M., Schmidt, B. and Neupert, W. 1982. *Eur. J. Biochem.* 125, 109–116.
20. Gasser, S. M., Daum, G. and Schatz, G. 1982. *J. Biol. Chem.* 257, 13034–13041.
21. Kolanski, D. M., Conboy, J. G., Fenton, W. A. and Rosenberg, L. E. 1982. *J. Biol. Chem.* 257, 8467–8471.
22. Freitag, H., Janes, M. and Neupert, W. 1982. *Eur. J. Biochem.* 126, 197–202.
23. Mihara, K., Blobel, G. and Sato, R. 1982. *Proc. Natl. Acad. Sci. USA* 79, 7102–7106.
24. Gasser, S. M. and Schatz, G. 1983. *J. Biol. Chem.* 258, 3427–3430.
25. Kaput, J., Goltz, S. and Blobel, G. 1982. *J. Biol. Chem.* 257, 15054–15058.
26. Reid, G. A., Yonetani, T. and Schatz, G. 1982. *J. Biol. Chem.* 257, 13068–13074.
27. Pfanner, N. and Neupert, W. 1985. *EMBO J.* 4, 2819–2825.
28. Zwizinski, C., Schleyer, M. and Neupert, W. 1983. *J. Biol. Chem.* 258, 4071–4074.
29. Pfanner, N. and Neupert, W. 1986. *FEBS Lett.* 209, 152–156.
30. Eilers, M., Oppliger, W. and Schatz, G. 1987. *EMBO J.* 6, 1073–1077.
31. Chen, W.-J. and Douglas, M. C. 1987. *Cell* 49, 651–658.

32. Kleene, R., Pfanner, N., Pfaller, R., Link, T.A., Sebald, W., Neupert, W. and Tropschug, M. 1987. *EMBO J.* 6, 2627–2633.
33. Hartl, F.-U., Ostermann, J., Pfanner, N., Tropschug, M., Guiard, B. and Neupert, W. 1987. In: *Cytochrome Systems: Molecular Biology and Energetics* (S. Papa et al., eds.), Plenum Publ. Corp., New York, in press.
34. Pfanner, N., Tropschug, M. and Neupert, W. 1987. *Cell* 49, 815–823.
35. Verner, K. and Schatz, G. 1987. *EMBO J.* 6, 2449–2456.
36. Rothmann, J.E. and Kornberg, R.D. 1986. *Nature* 322, 209–210.
37. Grossmann, A., Bartlett, S. and Chua, N.H. 1980. *Nature* 285, 625–628.
38. Flügge, U.I. and Hinz, G. 1986. *Eur. J. Biochem.* 160, 563–570.
39. Pain, D. and Blobel, G. 1987. *Proc. Natl. Acad. Sci. USA* 84, 3288–3292.
40. Hansen, W., Garcia, P.D. and Walter, P. 1986. *Cell* 45, 397–406.
41. Mueckler, M. and Lodish, H.F. 1986. *Nature* 322, 549–552.
42. Rothblatt, J.A. and Meyer, D.I. 1986. *EMBO J.* 5, 1031–1036.
43. Waters, M.G. and Blobel, G. 1986. *J. Cell Biol.* 102, 1543–1550.
44. Schlenstedt, G. and Zimmermann, R. 1987. *EMBO J.* 6, 699–703.
45. Wiech, H., Sagstetter, M., Müller, G. and Zimmermann, R. 1987. *EMBO J.* 6, 1011–1016.
46. Geller, B.L., Movva, N.R. and Wickner, W. 1986. *Proc. Natl. Acad. Sci. USA* 83, 4219–4222.
47. Yamane, K., Ichihara, S. and Mizushima, S. 1987. *J. Biol. Chem.* 262, 2358–2362.
48. Roise, D., Horvath, S.J., Tomich, J.M., Richards, J.H. and Schatz, G. 1986. *EMBO J.* 5, 1327–1334.

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