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Review

Catalytic properties of Na^+-translocating V-ATPase in *Enterococcus hirae*

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Abstract

V-ATPases make up a family of proton pumps distributed widely from bacteria to higher organisms. We found a variant of this family, a Na^+-translocating ATPase, in a Gram-positive bacterium, *Enterococcus hirae*. The Na^+-ATPase was encoded by nine *ntp* genes from F to D in an *ntp* operon (*ntpFIKECGABDHJ*): the *ntpJ* gene encoded a K^+ transporter independent of the Na^+-ATPase. Expression of this operon, encoding two transport systems for Na^+ and K^+ ions, was regulated at the transcriptional level by intracellular Na^+ as the signal. Structural aspects and catalytic properties of purified Na^+-ATPase closely resembled those of other V-type H^+-ATPases. Interestingly, the *E. hirae* enzyme showed a very high affinity for Na^+ at catalytic reaction. This property enabled the measurement of ion binding to this ATPase for the first time in the study of V- and F-ATPases. Properties of Na^+ binding to V-ATPase were consistent with the model that V-ATPase proteolipids form a rotor ring consisting of hexamers, each having one cation binding site. We propose here a structure model of Na^+ binding sites of the enzyme.

Keywords: Na^+-ATPase; V-ATPase; Na^+ binding; Na^+ binding site; Structure model; *Enterococcus hirae*

1. Introduction

Ion-motive adenosine triphosphatases (ATPases) that do not form phosphorylated intermediates are divided into two types: V_0V_1-type ATPase (V-ATPase) and F_0F_1-type ATPase (F-ATPase). V-ATPases are known as the proton pumps that acidify inside various organelles and energize plasma membranes in eukaryotic cells [1–3]. This acidification plays very important roles in many aspects of physiological functions [1–5]. F-ATPase functions as an ATP synthase in mitochondria, chloroplasts and oxidative bacteria [6,7]. Both ATPases are similar multisubunit enzymes consisting of a hydrophilic catalytic portion (V_1 and F_1, respectively) and a membrane-embedded portion (V_0 and F_0). In both cases, energy transfer between ATP hydrolysis/synthesis and proton movement requires three catalytic sites in the catalytic moiety (V_1 and F_1) and multiple proton-translocating proteolipids in the membrane-embedded portion (V_0 and F_0) [6–9].

A variety of primary sodium pumps have evolved in organisms living in high salinity or high pH [10]. In the fermentative eubacterium *Enterococcus hirae*,

Abbreviations: DCCD, *N,N′*-dicyclohexylcarbodiimide; EDTA, ethylenediaminetetraacetic acid

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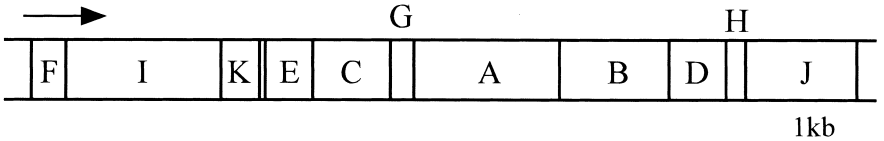
we found a Na^+-translocating V-ATPase that extrudes sodium ions from the cytoplasm and generates the Na^+ electrochemical gradient by using the energy of ATP. This sodium pump plays an important role in maintaining the sodium homeostasis of this bacterium in an alkaline environment. Taking advantage of the Na^+-coupled enzyme, we are now going to elucidate the mechanism of energy coupling of the V-ATPase. In this article we summarize the function and structure of *E. hirae* V-type Na^+-ATPase.

2. Na^+-ATPase (*ntp*) operon

2.1. Gene organization

Na^+-ATPase is encoded by an *ntp* gene cluster (*ntp* operon) consisting of 11 *ntp* genes: *ntpFIKEC-GABDHJ* (Fig. 1A). The Na^+-ATPase was purified from the membranes of cells in which the amount of Na^+-ATPase was increased by introducing this *ntp* operon [11,12]. Purified Na^+-ATPase consists of nine polypeptides, which were assigned to the *ntp* gene products from *ntpF* to *ntpD*. The amino acid sequences of the NtpA (69 kDa), NtpB (52 kDa) and NtpK (16 kDa proteolipid) subunits, the major subunits of this ATPase complex, were homologous (48–60% identity) to those of the A, B and *N,N′*-dicyclohexylcarbodiimide (DCCD) binding proteolipid subunits, respectively, of V-ATPases from various origins. The other six Ntp proteins (F, I, E, C, G, and D) are counterparts of eukaryotic V-ATPases, although the similarities between their amino acid sequences (35–50%) were only moderate (Fig. 1B). V-ATPase subunits similar to the *ntpH* and *ntpJ* gene products have not been found. As there is no strong Shine–Dalgarno sequence upstream of the mini *ntpH* gene, we now consider that *ntpH* is not an open reading frame. Interestingly, the *ntpJ* gene encodes a 49 kDa hydrophobic component of the K^+ uptake system (KtrII), and NtpJ is not mechanically linked with the Na^+-ATPase complex [13]. We speculate that the KtrII (NtpJ) transport system is a secondary Na^+/K^+ symporter.

A



B

V-type Na^+-ATPase from *E. hirae* (kDa)		Subcomplex	V-type H^+-ATPase from *S. cerevisiae* (kDa)		Subcomplex [a]
A	(66)	V_1	Vma1p	(69)	V_1
B	(51)	V_1	Vma2p	(60)	V_1
C	(38)	V_1	Vma6p	(36)	V_0
D	(27)	V_1	Vma8p	(32)	V_1
E	(23)	V_1	Vma4p	(27)	V_1
F	(14)	V_1	Vma10p	(13)	V_1
G	(11)	V_0?	Vma7p	(14)	V_1/V_0
H	(7)	---	---	---	---
I	(76)	V_0	Vph1p	(100)	V_0
J	(49)	---	---	---	---
K	(16)	V_0	Vma3p	(17)	V_0

Fig. 1. Organization of the *E. hirae* Na^+-ATPase (*ntp*) operon. (A) Structure of the *ntp* operon. The *ntp* operon is composed of 11 genes: *ntpF, I, K, E, C, G, A, B, D, H*, and *J*. The arrow indicates the transcriptional direction. (B) Similarities between Na^+-ATPase subunits (*ntp* gene products) and *Saccharomyces cerevisiae* V-ATPase subunits. [a]The assignment to subcomplex (V_1 or V_0) of *S. cerevisiae* V-ATPase subunits was taken from [23].

2.2. Gene expression

The *E. hirae* Na^+-ATPase level was not constant [14]. The Na^+-ATPase was induced when cells were grown on media rich in sodium, particularly under conditions that limit the generation of a proton gradient [15]. Western blotting and Northern blotting experiments revealed a substantial correlation of the amount of Na^+-ATPase and expression of the *ntp* operon [16]. Even under limited Na^+ concentrations, monensin or gramicidin D, rendering the membrane permeable to Na^+, significantly increased the amount of Na^+-ATPase and the mRNAs for the *ntp* operon. Furthermore, the *ntp* promoter activity was activated by Na^+ but not by Li^+ [17]. These findings suggest that the Na^+-ATPase is induced at the transcriptional level by an increase in the cytoplasmic Na^+ concentration as the signal, presumably via the cytoplasmic Na^+-specific sensing system.

2.3. Physiology

All living cells extrude Na^+ from the cytosol and accumulate high concentrations of K^+ into the cytosol for the homeostasis of K^+ and Na^+. In *E. hirae* grown at acidic pH, the proton electrochemical gradient is generated by proton extrusion via the F-type H^+-ATPase [18], of which the activity is optimal at pH 6–6.5. This H^+ gradient drives an efflux of Na^+ via the Na^+/H^+ antiporter and an influx of K^+ via the KtrI transport system [19]. However, this proton gradient is drastically decreased at environmental pHs above 8 [20,21]. Under these alkaline growth conditions, the Na^+/H^+ antiporter and the KtrI do not operate. Therefore, K^+ flows out from and Na^+ flows into the cytoplasm by diffusion. An increase in the intracellular Na^+ level stimulates the expression of an *ntp* operon, making the cell able to maintain the homeostasis of K^+ and Na^+ concentrations under alkaline conditions.

3. Structure of the Na^+-ATPase

Our current model for the architecture of the *E. hirae* V-ATPase is shown in Fig. 2. Densitometric analysis by SDS–PAGE of purified Na^+-ATPase suggested that the A, I, B, C, D, E, F, K, and G subunits occurred in a molar ratio of 3:1–2:3:1:1:3:2–3:4–6:1. The V_0V_1 complex was separated by Mg^{2+} chelation with ethylenediaminetetraacetic acid (EDTA) to V_1 and V_0 moieties. In *E. hirae* V-ATPase, six hydrophilic subunits, A, B, C, D, E, and F, were released from the membrane-embedded V_0 portion by EDTA treatment and the G, I, and K subunits were not [12]. Therefore, it is likely that the V_1 moiety consists of A, B, C, D, E, and F subunits.

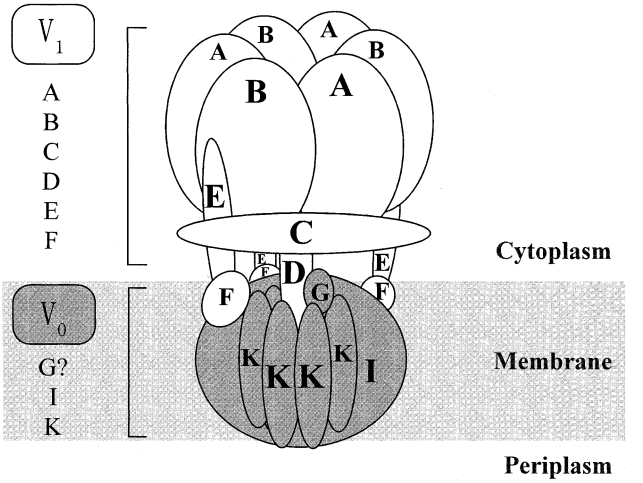


Fig. 2. Schematic structure model of *E. hirae* V-type Na^+-ATPase. *E. hirae* V-ATPase is composed of two large multisubunit subcomplexes designated V_1 and V_0. The V_1 portion (shown in white) consists of A, B, C, D, E, and F, and the V_0 portion (shaded) consists of G, I, and K. The existence of a central flat stalk, a few secondary stalks and a slender subunit perpendicular to the stalk have been observed in electron micrographs of purified Na^+-ATPase.

Since release of the D, E, and F subunits from the V_0 moiety was imperfect, these subunits may associate with the stalk region between the V_1 and V_0 sectors. It is reasonable that both the I and K subunits constitute the V_0 moiety, because the amino acid sequences of these subunits are hydrophobic. However, NtpG is a small (11 kDa) hydrophilic protein, and it has been reported that an NtpG homologous protein (yeast Vma7p) associates with both the V_1 and V_0 portions [22,23]. Further investigation is required for the assignment of the G subunit to the V_1 or V_0 portion.

The projected structure of purified Na^+-ATPase was observed by electron microscopy [24]. Besides a central flat stalk, a few secondary stalks were observed at the interface that connects the headpiece

V_1 and the membrane-bound part V_0 of the complex. These secondary stalks are likely to be the stator. A slender subunit perpendicular to the stalk was observed between V_1 and V_0 in many images of the enzyme. The height and width of this enzyme molecule were approximately 25 nm and 15 nm, respectively. These molecular images closely resembled those of *Clostridium fervidus* V-ATPase [25] and yeast V-type H^+-ATPase [26].

4. Catalytic properties of the Na^+-ATPase

4.1. ATPase activity

The Na^+-stimulated ATPase activity of the purified ATPase was maximal at pH 8–9 but not detectable at pH 6 [24]. At pH 8–9, the ATP hydrolytic activity of purified enzyme was tightly coupled with Na^+ or Li^+ but not K^+, Cs^+ or Ca^{2+}. The kinetics of ATP hydrolysis showed at least two different affinities of Na^+ (K_m values of 20 μM and 4 mM) or Li^+ (K_m values of 60 μM and 3.5 mM), and probably one more [11,12]. These different affinities for cations of the ATPase are probably linked with the mechanism, but its meaning remains unsolved.

4.2. Inhibitors

Azide (a specific inhibitor of F-ATPase) and vanadate (a specific inhibitor of P-ATPase that forms the phosphorylated intermediates) had no significant effect on the Na^+-ATPase. ATPase activity of purified enzyme was inhibited by V-ATPase inhibitors such as nitrate ($K_i = 37$ mM) and *N*-ethylmaleimide ($K_i = 0.2$ mM) but not by concanamycin A, a macrolide antibiotic that powerfully inhibits the V-ATPase [27]. Destruxin B, a peptide antibiotic that may attack the V_1 catalytic portion of V-ATPase [28], was effective against *E. hirae* Na^+-ATPase ($K_i = 30$ μM) as well as the eukaryotic V-ATPases. Thus, the effects of various compounds, except for concanamycin A, on Na^+-ATPase are in good accord with the features of V-ATPase.

Amiloride is known to be a potent inhibitor of many Na^+-coupled transport systems [29], including Na^+ channels, Na^+/H^+ antiporter, and the Na^+-driven flagellar motors [30]. However, this inhibitor was not effective against *E. hirae* V-type Na^+-ATPase. DCCD inhibited the purified enzyme in a pH-dependent manner, binding covalently to acidic amino acid residue (likely Glu-139) in NtpK proteolipids. The inactivation of the ATPase activity by DCCD is specifically prevented by the presence of Na^+ or Li^+ [12], as has been observed in the F-type Na^+-ATPases from *Propionigenium modestum* [31] and *Acetobacterium woodii* [32], suggesting that the Na^+ binding site overlaps with the DCCD-reactive site.

4.3. Na^+ uptake activity

When purified *E. hirae* Na^+-ATPase was incorporated into the liposomes, ATP-driven Na^+ uptake was observed. Na^+ uptake was blocked by nitrate and monensin but accelerated by carbonyl cyanide *m*-chlorophenylhydrazone and valinomycin, demonstrating that ATP-driven Na^+ movement by *E. hirae* V-ATPase is electrogenic. Furthermore, V_0 liposomes catalyzed electrogenic Na^+ uptake in response to potassium diffusion potential (Δt, inside negative). Δt-induced $^{22}Na^+$ uptake by V_0 liposomes was inhibited by 0.5 mM DCCD in the absence of Na^+ but not in the presence of 2 mM Na^+ [12]. These findings suggest that V_0 maintains the ability to bind Na^+ to the cation binding site and to transport Na^+ to the opposite side.

5. Properties and structure model of Na^+ binding sites

Most recently, we examined $^{22}Na^+$ binding of *E. hirae* V-type Na^+-ATPase as the first direct demonstration of cation binding in the studies of V- and F-ATPases [33]. The kinetics of Na^+ binding to purified V-ATPase suggested 6 ± 1 Na^+ bound/enzyme molecule, with a single high affinity ($K_{d\,Na^+} = 15 \pm 5$ μM). The $K_{d\,Na^+}$ value is similar to the lower (20 μM) of the two K_m values for Na^+ of the ATPase activity [11,12,33]. The number of cation binding sites is consistent with the model that V-ATPase proteolipids form a rotor ring consisting of hexamers, each having one cation binding site [34,35]. The Na^+ binding to purified molecules was mostly prevented by preincubation with DCCD but not by ADP, ATP analogs or other inhibitors of V-ATPase. Release of

the bound $^{22}Na^+$ from purified molecules in a chasing experiment showed two phases: a fast component (about two thirds of the total amount of bound Na^+; $k_{exchange} > 1.7$ min^{-1}) and a slow component (about one third of the total; $k_{exchange} = 0.16$ min^{-1}). It was considered that the fast and slow components correspond to four and two sites in the six binding sites of the Na^+-ATPase, respectively. Therefore, it appears that the four sites (fast component) are freely accessible from the aqueous phase and the two sites (slow component) are difficult to access. This slow component changed to the fast component by adding ATP or adenosine 5′-*O*-(3-thiotriphosphate), suggesting that the slow component is involved in the transport reaction [33].

Based on the findings described, we propose a structure model of Na^+ binding sites of *E. hirae* Na^+-ATPase as follows. NtpK proteolipids form a rotor ring consisting of hexamers, each having one high-affinity Na^+ binding site ($K_{d\ Na^+} = 15 \pm 5$ μM) (Fig. 3). Two Na^+ binding sites (slow component) of the NtpK rotor are covered by NtpI, which is another major subunit of the V_0 portion, and are subject to steric hindrance. Therefore, the exchange rate becomes slow ($k_{exchange} = 0.16$ min^{-1}). The other four Na^+ binding sites (fast component) of the NtpK rotor are readily accessible from the cytoplasmic solution and exchange Na^+ easily ($k_{exchange} > 1.7$ min^{-1}) (Fig. 3).

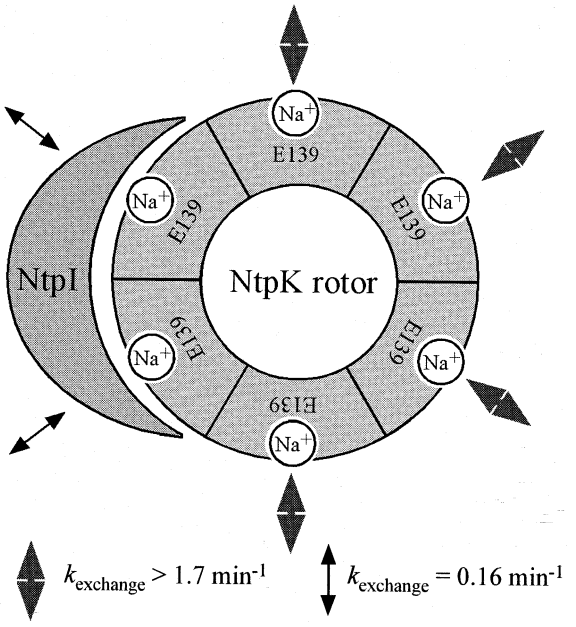


Fig. 3. Model for Na^+ binding sites of *E. hirae* V-type Na^+-ATPase viewed from the cytoplasm. Six NtpK subunits are depicted as a ring (rotor), each having one Na^+ binding site (Glu-139). These sites bind Na^+ with high affinity ($K_{d\ Na^+} = 20 \pm 5$ μM). The Na^+ binding sites (four sites) of NtpK that do not adjoin with NtpI are freely accessible from the cytoplasmic solution ($k_{exchange} > 1.7$ min^{-1}). The other Na^+ binding sites (two sites) of NtpK covered with NtpI are difficult to access from the cytoplasmic solution because of steric hindrance ($k_{exchange} = 0.16$ min^{-1}).

6. Mechanism

We think that there must be a common energy-transducing principle between V- and F-ATPase molecules. The 'rotation catalysis' mechanism [36], which has been experimentally verified in F-ATPase [37–40], is applicable to V-ATPase; the energy of ATP hydrolysis is converted into physical force in the form of rotation of the 'γ-like' subunit, with three ATP hydrolyses/rotation. The important question is how the physical rotation and ion transport are connected, and models for the mechanism of ion translocation through the F_0 portion have been proposed [8,41–45]. In F-ATPase, a great deal of evidence indicates that the c and a subunits interact directly and are necessary for cation translocation [41,42,44,46]. Therefore, researchers speculate that the cation is transported at the interface of the c and a subunits by rotation energy of the c subunit rotor ring [8,43–45]. In yeast V-ATPase, a 100 kDa subunit (Vph1p) similar to NtpI is suggested to be important for H^+ translocation in the V_0 portion [47]. Therefore, we speculate that the hexamer rotor of NtpK rotates and that Na^+ is serially transported at the interface between NtpK and NtpI, similar to the proposed mechanism of F-ATPase [8,45], but further investigation including structure determination is required.

7. Difference between V- and F-ATPases

The following points are regarded as highly relevant with regard to differences between V- and F-ATPases in physiological function:

1. The affinity for the ion at binding sites. The apparent K_m (about 0.8 mM) for Na^+ of *P. modes-*

tum F-ATPase [48] is higher than the low K_m or $K_{d\ Na^+}$ (about 20 μM) values of *E. hirae* V-ATPase. The low affinity for the coupling ion (Na^+ in this case) of the F-ATPase is advantageous for synthesizing ATP, because Na^+ is easily released in the cytosol after being transported from the periplasm driven by the electrochemical gradient. In contrast, *E. hirae* Na^+-ATPase appears to have great difficulty in releasing Na^+ in the cytosol, which should bring about product inhibition against synthesizing ATP. Instead, the high affinity for the coupling ion of the V-ATPase should be advantageous for thoroughly extruding the ion from cytosol.

2. The number of binding sites of the proteolipid rotor. The γ subunit of F-type ATPase or 'γ-like' subunit of V-ATPase rotates 120° by one ATP hydrolysis [40]. Since the ion binding sites of the proteolipid rotor of F-ATPase and V-ATPase are 12 and six, respectively [8,34,35,45], a 120° rotation to synthesize one ATP appears to necessitate the transport of four ions for F-ATPase and two ions for V-ATPase. When V-ATPase synthesizes ATP, it requires an electrochemical gradient of the coupling ion that is two-fold larger than that of F-ATPase.
3. The pore complex of V_0 moiety. It is noteworthy that in contrast to the *E. hirae* Na^+-ATPase and F-ATPases the pore complex of eukaryotic V-ATPases contain three isoforms of the proteolipid [49]. All of them seem to contribute to the mechanism of proton translocation.

Thus, V-ATPase may have evolved to work as an ATP hydrolase by changing the affinity for the ion, the gear ratio of the proteolipid rotor, and the rotor complex in eukaryotic cells.

8. Conclusion

The Na^+-coupled enzyme is expected to be very useful in the investigation of the energy-coupling mechanism of the V- and F-ATPases. *E. hirae* Na^+-ATPase is a unique variant of V-type ATPase, which pumps out Na^+ using energy of ATP. By utilizing this advantage, we characterized the Na^+ binding reaction of the V_0 portion for the first time and proposed a structure model of Na^+ binding sites. However, it is absolutely essential to obtain structure information of the enzyme at atomic resolution by X-ray crystallography in order to understand details of the reaction mechanism and energy-coupling mechanism. We are currently attempting to examine *E. hirae* V-ATPase using X-ray crystallography.

Acknowledgements

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References

[1] N. Nelson, L. Taiz, Trends Biochem. Sci. 14 (1989) 113–116.
[2] N. Nelson, Biochim. Biophys. Acta 1100 (1992) 109–124.
[3] H. Wieczorek, D. Brown, S. Grinstein, J. Ehrenfeld, W.R. Harvey, BioEssays 21 (1999) 637–648.
[4] Y. Anraku, N. Umemoto, R. Hirata, Y. Wada, J. Bioenerg. Biomembr. 21 (1989) 589–604.
[5] Y. Moriyama, A. Yamamoto, H. Yamada, Y. Tashiro, M. Takahashi, M. Maeda, M. Futai, J. Biol. Chem. 270 (1995) 11424–11429.
[6] M. Futai, T. Noumi, M. Maeda, Annu. Rev. Biochem. 58 (1989) 111–136.
[7] A.E. Senior, Annu. Rev. Biophys. Chem. 19 (1990) 7–41.
[8] T.H. Stevens, M. Forgac, Annu. Rev. Cell Dev. Biol. 13 (1997) 779–808.
[9] W. Junge, H. Lill, S. Engelbrecht, Trends Biochem. Sci. 22 (1997) 420–423.
[10] P. Dimroth, Microbiol. Rev. 51 (1987) 320–340.
[11] T. Murata, K. Takase, I. Yamato, K. Igarashi, Y. Kakinuma, J. Biol. Chem. 272 (1997) 24885–24890.
[12] T. Murata, K. Takase, I. Yamato, K. Igarashi, Y. Kakinuma, J. Biochem. (Tokyo) 272 (1999) 24885–24890.
[13] T. Murata, K. Takase, I. Yamato, K. Igarashi, Y. Kakinuma, J. Biol. Chem. 271 (1996) 10042–10047.
[14] N. Kinoshita, T. Unemoto, H. Kobayashi, J. Bacteriol. 158 (1984) 844–848.
[15] Y. Kakinuma, K. Igarashi, FEBS Lett. 271 (1990) 97–101.
[16] T. Murata, I. Yamato, K. Igarashi, Y. Kakinuma, J. Biol. Chem. 271 (1996) 23661–23666.
[17] M. Ikegami, M. Kawano, K. Takase, I. Yamato, K. Igarashi, Y. Kakinuma, FEBS Lett. 454 (1999) 67–70.
[18] A. Abrams, in: A.N. Martonosi (Ed.), Enzymes in Biological Membranes, Vol. 4, 2nd edn., Plenum Press, New York, 1985, pp. 177–193.
[19] Y. Kakinuma, in: E.P. Bakker (Ed.), Alkali Cation Trans-

port Systems in Prokaryotes, CRC Press, Boca Raton, FL, 1993, pp. 277–290.
[20] Y. Kakinuma, J. Bacteriol. 169 (1987) 3886–3890.
[21] Y. Kakinuma, K. Igarashi, J. Biol. Chem. 263 (1988) 14166–14170.
[22] L.A. Graham, K.J. Hill, T.H. Stevens, J. Biol. Chem. 269 (1994) 25974–25977.
[23] L.A. Graham, T.H. Stevens, J. Bioenerg. Biomembr. 31 (1999) 39–47.
[24] Y. Kakinuma, I. Yamato, T. Murata, J. Bioenerg. Biomembr. 31 (1999) 7–14.
[25] E.J. Boekema, T. Ubbink-Kok, J.S. Lolkema, A. Brisson, W.N. Konings, Proc. Natl. Acad. Sci. USA 94 (1997) 14291–14293.
[26] S. Wilkens, E. Vasilyeva, M. Forgac, J. Biol. Chem. 274 (1999) 31804–31810.
[27] E.J. Bowman, A. Siebers, K. Altendorf, Proc. Natl. Acad. Sci. USA 85 (1988) 7972–7976.
[28] M. Muroi, N. Shiragami, A. Takatsuki, Biochem. Biophys. Res. Commun. 205 (1994) 1358–1365.
[29] D.J. Benos, Am. J. Physiol. 242 (1982) 131–145.
[30] S. Sugiyama, E.J. Cragoe, Y. Imae, J. Biol. Chem. 263 (1988) 8215–8219.
[31] C. Kluge, P. Dimroth, J. Biol. Chem. 268 (1993) 14557–14560.
[32] R. Heise, V. Müller, G. Gottschalk, Eur. J. Biochem. 206 (1992) 553–557.
[33] T. Murata, K. Igarashi, Y. Kakinuma, I. Yamato, J. Biol. Chem. 275 (2000) 13415–13419.
[34] H. Arai, M. Berne, M. Forgac, J. Biol. Chem. 262 (1987) 11006–11011.
[35] T. Pali, M.E. Finbow, A. Holzenburg, J.B.C. Findlay, D. Marsh, Biochemistry 34 (1995) 9211–9218.
[36] P.D. Boyer, Biochim. Biophys. Acta 1140 (1993) 215–250.
[37] T.M. Duncan, V.V. Bulygin, Y. Zhou, M.L. Hutcheon, R.L. Cross, Proc. Natl. Acad. Sci. USA 92 (1995) 10964–10968.
[38] H. Noji, R. Yasuda, M. Yoshida, K. Kinosita, Nature 386 (1997) 299–302.
[39] D. Sabbert, S. Engelbrecht, W. Junge, Nature 381 (1996) 623–625.
[40] R. Yasuda, H. Noji, K. Kinosita, M. Yoshida, Cell 93 (1998) 1117–1124.
[41] O.Y. Dmitriev, K. Altendorf, R.H. Fillingame, Eur. J. Biochem. 233 (1995) 478–483.
[42] S.B. Vik, B.J. Antonio, J. Biol. Chem. 269 (1994) 30364–30369.
[43] T. Elston, H. Wang, G. Oster, Nature 391 (1998) 510–514.
[44] G. Kaim, P. Dimroth, EMBO J. 17 (1998) 5887–5895.
[45] P. Dimroth, H. Wang, M. Grabe, G. Oster, Proc. Natl. Acad. Sci. USA 96 (1999) 4924–4929.
[46] S. Singh, P. Turina, C. Bustamante, D.J. Keller, R. Capaldi, FEBS Lett. 397 (1996) 30–34.
[47] X.H. Leng, M.F. Manolson, Q. Liu, M. Forgac, J. Biol. Chem. 271 (1996) 22487–22493.
[48] W. Laubinger, P. Dimroth, Biochemistry 27 (1988) 7531–7537.
[49] R. Hirata, L.A. Graham, A. Takatsuki, T.H. Stevens, Y. Anraku, J. Biol. Chem. 272 (1997) 4795–4803.