

Fig. 4 Channel from OMM. Single channel currents were measured in symmetrical 150 mM KCl, from a mitochondriaattached patch, at +40 mV. These channels display a mean conductance of 347 ± 26 pS.

this value might correspond to the single channel conductance of 480 pS (100 mM KCl), found for the VDAC after reconstitution in planar lipid bilayers7.

To our knowledge, this is the first report of patch-clamp studies of the IMM (the patch-clamping of the OMM was recently reported⁸), and of the presence of a high conductance ion channel in it. The possible existence of an inner membrane protein, able to translocate anions electrophoretically, has already been suggested⁹⁻¹². Unfortunately the turnover of this anion channel is not yet known, though it is known to be maximally activated at alkaline pH and to be regulated also by magnesium and calcium ions. These characteristics and the lack of effect of quinine¹² on the channel activity described here render it unlikely that they are the same channel. But until comparable data are available, and because of the different incubation and experimental conditions used by us, we cannot definitively rule out this possibility.

It is important to understand the possible physiological function and regulation of the IMM channel. The presence of the channel in most membrane patches, together with the high conductivity displayed, suggests a non-trivial role in the regulatory processes of the IMM and of the mitochondrion in general, many of which are not yet fully appreciated or understood^{12,13} Indeed, with the particular properties of the IMM component described here, several functions could be feasible. This channel could be regarded as an intrinsic uncoupling protein analogous to, and with similar function to, that of brown fat mitochondria¹⁴. Thus, the IMM channel could be of key importance in providing heat in tissues other than brown fat.

Mitochondria are known to undergo finely tuned volume changes¹⁵. In line with that envisaged for the anion channel¹², the IMM channel could represent a safeguard mechanism for the maintenance of volume homeostasis of mitochondria. Such control is extremely important under normal but especially under pathological conditions, such as ischemia¹², where the excessive swelling of the matrix impairs those mitochondrial functions essential for cell survival. Undoubtedly the high ion conductance of the IMM channel renders it highly suitable for such a role.

Finally, another tantalizing possibility, which involves mitochondrial biogenesis, must be taken into consideration. The majority of mitochondrial proteins are synthesized in the cytoplasm and hence have to be imported into the organelle via a mechanism which is not known in detail¹³. Hurt and van Loon¹⁶ have posed the question of whether channels can mediate such transport. As a proteinaceous component of the OMM has recently been found to be part of the import apparatus¹⁷, it will be of interest to ascertain whether the IMM has a similar role and if it is involved in the continuous traffic of macromolecules occurring between the organelle and the cytoplasm¹³.

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In this paper the scale on Fig. 1b was printed incorrectly and Fig. 2 was shown upside down through no fault of the authors. The two figures are correct as printed here.