



Synthesis and Characterization of Novel Ionoconductor Gels for Biomedical Applications in Space

Paola Romagnoli,^a Maria Luisa Di Vona,^a Livio Narici,^b Walter G. Sannita,^{c,d}
Enrico Traversa,^{a,*} and Silvia Licoccia^{a,*z}

^aDipartimento di Scienze e Tecnologie Chimiche and ^bDipartimento di Fisica, Università di Roma Tor Vergata, 00133 Rome, Italy

^cCentro Farmaci Neuroattivi-Dipartimento di Scienze Motorie, Università di Genova, 16132 Genova, Italy

^dDepartment of Psychiatry, State University of New York, Stony Brook, New York, 11764-8101 USA

Under the framework of the project Anomalous Long Term Effects in Astronauts, an experiment to study the risk for functional brain anomalies due to cosmic radiation during long manned missions, a new gel-type polymer electrolyte membrane for recording bioelectric signals in space has been developed. Ionic conducting gels have been formed by immobilizing liquid solutions, containing LiX salts (X = ClO₄, CF₃SO₃) dissolved in 1,2-diethoxyethane (gly), using poly(methyl methacrylate) (PMMA) as the polymeric matrix. The electrical properties of these membranes have been studied using impedance spectroscopy. The membranes exhibit good mechanical and chemical stability and high conductivity at room temperature (10⁻³ to 10⁻⁴ S cm⁻¹). The highest conductivity value has been determined for membranes prepared from LiCO₄-gly-PMMA having molar composition 7.19/64.01/28.80%. Preliminary experiments on electroencephalogram signals recorded with this new gel showed that the recordings are almost identical to those measured simultaneously using a conventional apparatus.

© 2001 The Electrochemical Society. [DOI: 10.1149/1.1415726] All rights reserved.

Manuscript submitted March 1, 2001; revised manuscript received July 16, 2001. Available electronically November 2, 2001. This was Paper 861 presented at the Phoenix, Arizona, Meeting of the Society, October 20-27, 2000.

During the Apollo 11 mission, Edwin "Buzz" Aldrin made the first report of anomalous visual perceptions by astronauts. Since then, several experimental studies confirmed the correlation between the assured presence of particle flux, inside and outside the space station, and the phenomenon called Light Flash (LF), or more properly, "phosphenes anomalous perceptions." LF consists of an unexpected visual sensation that is perceived by the astronaut, after a period of dark adaptation, as faint spots or streaks of light in closed eyes. Currently, LF perception is probably the only functional anomaly directly caused by a single particle, although the real cause is still not clear. The mechanisms originating LF perception seem to involve the passage of a cosmic charged particle through the cosmonaut's visual system. Therefore, it is important to determine simultaneously the time, nature, energy, and trajectory of the particle passing through the cosmonaut's eyes, as well as the astronaut's LF observation time.^{1,2}

The international project called A.L.T.E.A. (Anomalous Long Term Effects in Astronauts) has been developed to study the possible temporary and/or permanent altered function of the astronaut's brain during long periods in space. Experiments on visual system responses are planned to monitor the status of the astronaut's central nervous system (CNS). Furthermore, studies on correlations between electrophysiological changes and passages of particles through the brain and/or the retina in the space-adapted CNS are to be performed. The aim of the project is to assess the origin of the anomalous LF perception.

The development of new techniques for monitoring brain functionality directly in space is a necessary step toward the success of the project. Our research has thus been directed to the development of new ionoconducting solid gels to be used as an interface between the skin and the actual electrical instrumentation used to produce an electroencephalogram (EEG). Owing to the peculiarity of this application, the main requirements for such gels are (i) to have conductivity comparable to that of the hydrogels used in conventional EEG recording (10⁻³ to 10⁻⁴ S cm⁻¹);³ (ii) to be completely nontoxic; (iii) to be homogeneous; (iv) to have good mechanical properties, e.g., ductility, resilience (elasticity), for easy handling; and (v) to exhibit good chemical and electrical stability.

These requirements can be met by a polymeric gel: such a sys-

tem is characterized by an elastic cross-linked network and by a fluid filling the interstitial space. The long polymeric network holds the liquid in place, giving the gel the desired mechanical properties. Since they are not brittle, polymers can form good interfacial contacts with electrode materials and, more importantly, maintain these contacts under stress. Many polymers exhibit a low but finite conductivity, which is a result of ion or electron hopping between localized sites and is regulated by segmental motion of the polymer chains.^{4,5}

The systems chosen in the present work are polymeric membranes formed by gelatinization of a liquid solution (lithium salts dissolved in a highly polar organic solvent) in a poly(methyl methacrylate) (PMMA) matrix.

The use of polymer electrolytes is well known in electrochemical devices such as sensors, batteries, and fuel cells.⁶ Membranes made of polymeric gels containing lithium salts are widely used for Li batteries since they couple the high energy, long life characteristics of the lithium process with the reliability and easy processing of the plastic configuration.^{7,8} Numerous studies on such advanced polymer electrolyte materials have been carried out in recent years,^{5,9-11} and lithium batteries have also been employed in biomedical devices such as cardiac pacemakers or neurostimulators.¹² However, to our knowledge, no report on the use in a biomedical application of a lithium-containing system where the membrane must be used at ambient conditions and in direct contact with the skin is known to date. The mechanical properties and nontoxic characteristics must be deeply modified for the present application.

In this work, we describe and discuss the synthesis and electrochemical characterization of newly developed gel-type membranes that combine appropriate mechanical properties with good ionic conductivity. Generally, the ion transport mechanism in these composite materials appears to be dominated by the liquid electrolyte, as demonstrated by the fact that the conductivity of the "solid" gel is not much lower than that of the liquid electrolyte constituent.

Experimental

All reagents (Aldrich) were reagent grade and were used without further purification. The preparative procedure developed involved the following sequence of steps:

1. The dissolution at room temperature of the selected salt in the given solvent.
2. The addition of the polymer component and its dispersion in the solution by stirring at room temperature.

* Electrochemical Society Active Member.

^z E-mail: licoccia@uniroma2.it

Table I. Composition and conductivity at room temperature of gel electrolyte membranes prepared in our laboratory.

Label	Electrolyte membrane	[Li ⁺] ^a (mol/L)	Molar composition (%)	Conductivity (S cm ⁻¹)
M1	LiClO ₄ -gly-PMMA	0.8	7.19-64.01-28.80	1.63 × 10 ⁻³
M2	LiClO ₄ -gly-PMMA	1.0	9.09-64.71-26.20	1.51 × 10 ⁻³
M3	LiClO ₄ -gly-PMMA	0.5	4.76-67.79-27.44	3.56 × 10 ⁻⁴
M4	LiClO ₄ -gly-PMMA	1.5	13.02-61.91-25.06	4.46 × 10 ⁻⁴
M5	LiClO ₄ -gly-PMMA*	0.8	7.19-64.01-28.80	7.70 × 10 ⁻⁴
M6	LiClO ₄ -gly-PMMA + HA	0.8	5.08-45.23-20.35-29.34	1.28 × 10 ⁻³
M7	LiCF ₃ SO ₃ -gly-PMMA	1.0	9.09-64.71-26.20	1.78 × 10 ⁻⁴
M8	LiCF ₃ SO ₃ -gly-PMMA	0.8	7.02-64.13-28.85	3.40 × 10 ⁻⁴

PMMA = 996.000 Mw

PMMA* = 350.000 Mw

gly = 1,2-diethoxyethane

HA = CH₃COOH

^aCalculated for the original solution of lithium salt in 1,2-diethoxyethane.

3. Heating at a selected temperature (~70°C) for promoting fast and complete dissolution of the polymer.

4. Cooling to room temperature to favor cross-linking in the membrane and gel formation.

The electrolyte gels were prepared by gelling in a PMMA matrix a solution of a lithium salt (LiClO₄, LiCF₃SO₃) in 1,2-diethoxyethane (gly). A typical preparation, described for a representative sample (M1) (see Table I), is as follows: LiClO₄ (0.64 g, 6.05 mmol) was dissolved in 1,2-diethoxyethane (7.6 mL). PMMA (2.28 g) was then added to the electrolyte solution. The mixture was heated to 70°C until complete gelatinization occurred. The gel was poured into a Petri dish, and samples with proper mechanical properties were obtained in 24-48 h. The membranes had an average thickness of 1-2 mm and were stored in closed vials at room temperature. The different compositions are listed in Table I with their conductivity values.

The ionic conductivity of the gels was measured by impedance spectroscopy performed on Teflon cells formed by sandwiching the given gel sample between two stainless steel (SS) blocking electrodes.

The measurements were carried out using a Solartron frequency response analyzer (model 1260) scanning over a 1 Hz to 100 kHz range. Data were processed with an appropriate fitting program.

For EEG recording, gelation was performed on the surface of an SS electrode. GRASS EEG gold electrodes with added commercial conducting gel were positioned at occipital locations (O1 and O2 of the 10-20 International System) with reference at Fz; the ground electrode was at the vertex (Cz). The electrodes M1 were positioned at the same locations, about 8 mm from the conventional electrodes directly in contact with the scalp.

Bipolar EEG recordings (subject in resting conditions, with eyes closed) were simultaneously obtained from conventional and M1 electrodes in 1 min epochs. The signal was processed off-line by power spectral analysis on consecutive 2 s epochs (after acquisition through multiplexed analog to digital conversion (ADC) processing), and the signal power values in the 0.5-100 Hz range were computed.

Results and Discussion

The synthetic strategy consisted of gelling in a polymer matrix a solution of the chosen electrolyte. Great care was devoted in the synthetic procedure to obtain homogeneous samples to avoid gel decomposition and to maintain a low impurity level.

Numerous salts of different alkali metals were examined. Since the major portion of ions present in tissue fluids and sweat are sodium, potassium, and chloride,³ the first salts tested were potassium chloride and sodium chloride, acetate, nitrite, and citrate. All sodium and potassium salts tested were rejected, either because of poor

solubility in the reaction mixture or because the mechanical properties of the resulting gel were not satisfactory. The use of lithium salts led to membranes with better performance, and LiClO₄ and LiCF₃SO₃ were chosen because they are nontoxic. The optimized procedure developed led to the formation of homogeneous and mechanically stable samples.

In our systematic approach, we considered various types of membranes formed by the different combinations of their components listed in Table I, where the labels used to identify the membranes and their conductivity values are also reported. Samples were prepared from PMMA in 1,2-diethoxyethane using LiClO₄, LiCF₃SO₃, or a protonic species (CH₃COOH) as electrolytes. Many studies have shown that the conductivity is critically affected by the physical properties of the solvent, such as viscosity, mobility, and dielectric constant, and by the concentration of the salt in the electrolyte.⁴ Low viscosity leads to high ionic mobility, thus maximizing conductivity. The solvating properties of 1,2-diethoxyethane and its low viscosity meet the needed requirements. The density of the membranes was determined to be ~100 kg/m³, *i.e.*, similar to that of the expanded foam that is used as the electrode backing material in conventional bioelectrical recording.¹³ Such density allows absorption of mechanical disturbances, thus minimizing motion artifacts.

The first important observation that can be made from the data in Table I is that the gels have a good ionic conductivity, in some cases exceeding 10⁻³ S cm⁻¹ at room temperature.

Figures 1 and 2 show typical impedance plots of some of the membranes studied. The linear trend of the impedance plots gives convincing evidence of good physical integrity of the membranes. Lack of homogeneity, such as that resulting by liquid loss, phase separation phenomena, or crystallization, would have been reflected by the occurrence of semicircle evolution in the high frequency region.⁸

Figure 1 shows the effect of varying the electrolyte component on the impedance plots of membranes derived from gels having the same molar concentration of lithium ions. The difference in counterion seems to be the discriminating factor, as shown by the highest value of conductivity measured for membrane M1 (containing LiClO₄) with respect to membrane M8 (containing LiCF₃SO₃). The addition of acetic acid did not substantially modify the performance of the membranes containing lithium perchlorate: the conductivity values of membranes M1 and M6 are comparable.

The electrolyte properties depend critically on the ratio of the three components, particularly the salt ratio. The effect of variation in lithium concentration is shown in Fig. 2. The conductivity of samples containing LiClO₄ shows the highest value for a salt concentration of 0.8 M. For low concentration values, the number of

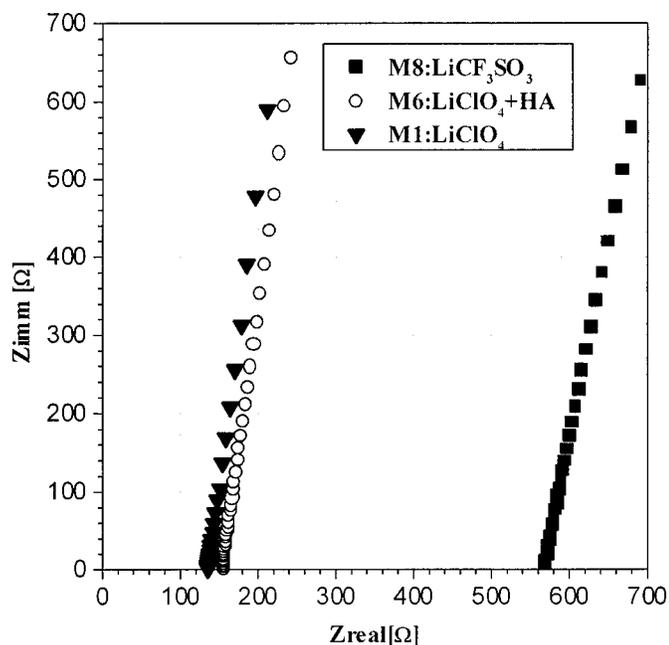


Figure 1. Impedance spectra of SS/LiX-gly-PMMA/SS cells at room temperature. Frequency range: 100 kHz to 1 Hz.

mobile charges is reduced in the system, whereas for high concentration values, the formation of ion pairs prevails over charged species in solution. Therefore, a concentration of 0.8 M in LiClO_4 (M1) was chosen for the gel preparation because of its optimal electrical characteristics among the systems examined.

The influence of the length of the polymeric chain on the electrical response of the membranes was also examined as shown by the data (Fig. 2) relative to sample M1 and M5, which have the same molar composition and differ in the average molecular weight of the PMMA used (996,000 for M1 and 350,000 for M5). The effect is not as important as that due to the variations in lithium

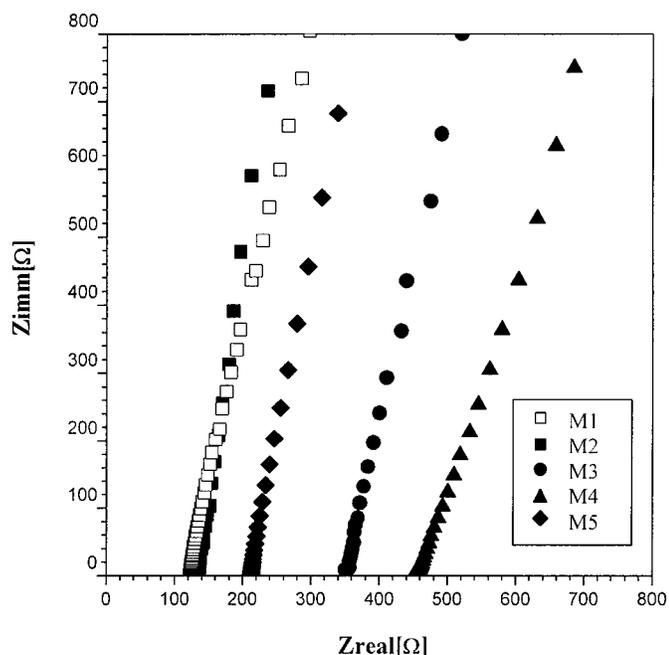


Figure 2. Impedance spectra of SS/LiClO₄-gly-PMMA/SS cell with different compositions at room temperature. Frequency range: 100 kHz to 1 Hz.

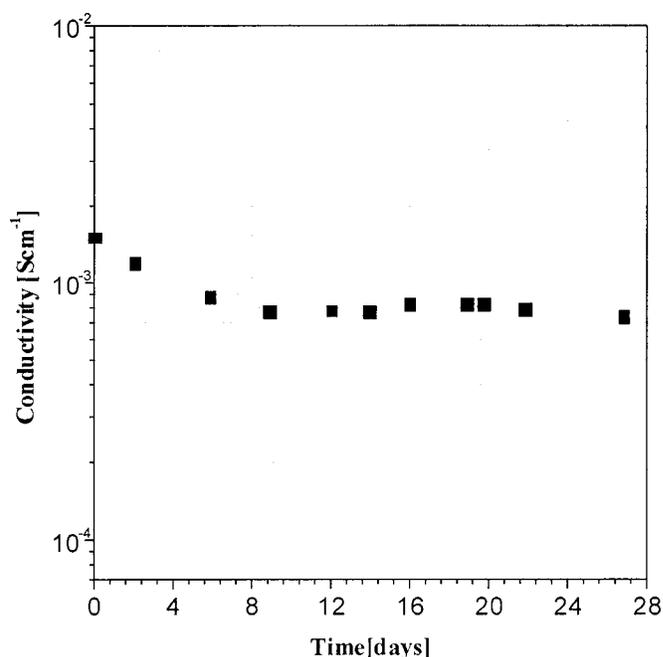


Figure 3. Time evolution of the room temperature conductivity of the LiClO_4 -gly-PMMA gel-type membrane. Data obtained by impedance spectroscopy.

concentration and may be attributed to the different mobilities of the polymeric chains, which affect the motion of the ions through the polymeric matrix (supported transport).⁸

Since the desired application will require long storage periods of the membranes, their electrical properties were monitored as a function of time. The general features of the impedance spectra were maintained over a period of one month. A plot of conductivity vs. storage time is shown in Fig. 3. After a decrease in the first week, which may be due to some syneresis phenomena, the conductivity values did not show any significant variation. The data confirm that the integrity and homogeneity of the sample are not affected by time and indicate that, although macroscopically solid, the gel-type membranes may benefit microscopically from a transport mechanism which is similar to that of their liquid components.

Samples of cerebral bioelectrical signals were recorded from healthy humans through M1 electrodes and were compared to those obtained via conventional dermal electrodes for human (EEG) recording. Figure 4 shows samples of EEG signals simultaneously recorded by conventional (top row in A, B, and C) and M1 electrodes (bottom row) from adjacent scalp locations. The patterns A refer to signals recorded with 1.0-100.0 Hz bandpass and a notch filter at 50 Hz, while patterns B refer to signals recorded with the same bandpass, but without the notch filter. The patterns C are examples of signal epochs with artifacts due to movement. The recordings obtained using both electrodes are almost identical. Figure 4 also reports the superimposed power spectra of the signals in A. The signals obtained using M1 electrodes show a peak at about 50 Hz.

Conclusions

New ionoconducting gels operating at ambient conditions were prepared and their electrical properties characterized. The membranes derived from gels based on lithium perchlorate, 1,2-diethoxyethane, and high average molecular weight PMMA showed high and stable conductivity values and almost identical electrical

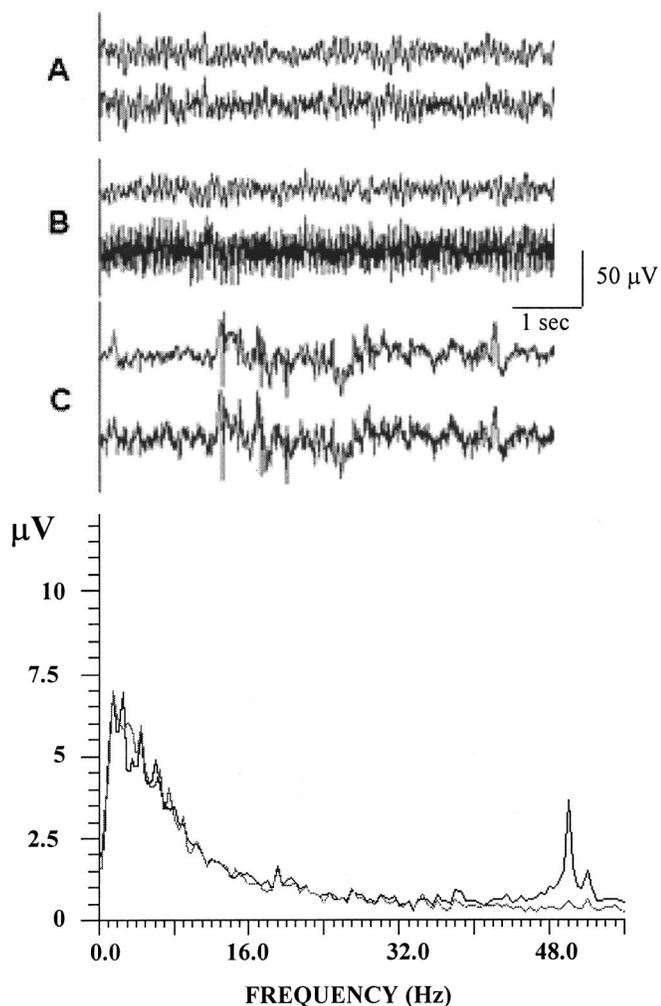


Figure 4. Comparison of bioelectric trace recordings obtained with the new polymer gel M1 (bottom traces) and with conventional apparatus (top traces).

responses in EEG measurements as those determined with conventional systems. Moreover, good mechanical stability and physical integrity were obtained for these polymeric gels.

The described unique electrical features make the gel-type electrolyte membranes very interesting substrates for the development of newly designed gels for biomedical applications.

Acknowledgments

The authors thank C. D'Ottavi for her valuable technical assistance. This work has been supported by Agenzia Spaziale Italiana and Ministero dell'Università e della Ricerca Scientifica e Tecnologica.

Università di Roma Tor Vergata assisted in meeting the publication costs of this article.

References

1. V. Bidoli, M. Casolino, M. P. De Pascale, G. Furano, A. Morselli, L. Narici, P. Picozza, E. Reali, R. Sparvoli, A. M. Galper, Yu. V. Ozerov, A. V. Popov, N. R. Vavilov, A. P. Alexandrov, S. V. Avdeev, V. G. Shabelnikov, G. Barbiellini, W. Bonvicini, N. Zampa, G. Mazzenga, M. Ricci, M. Boezio, P. Carlson, C. Fuglesang, P. Spillantini, and W. Sannita, in *Proceedings of the 2nd European Symposium on the Utilisation of the International Space Station*, ESTEC, Noordwijk, The Netherlands p. 505 (1998).
2. V. Bidoli, M. Casolino, M. P. De Pascale, G. Furano, A. Morselli, L. Narici, P. Picozza, E. Reali, R. Sparvoli, A. M. Galper, Yu. V. Ozerov, A. V. Popov, N. R. Vavilov, A. P. Alexandrov, S. V. Avdeev, Yu. Baturin, Yu. Budarin, G. Padalko, V. G. Shabelnikov, G. Barbiellini, W. Bonvicini, A. Vacchi, N. Zampa, G. Mazzenga, S. Bartalucci, M. Ricci, O. Adriani, P. Spillantini, M. Boezio, P. Carlson, C. Fuglesang, G. Castellini, and W. Sannita, *Adv. Space Res.*, **25**, 2075 (2000).
3. J. Jossinet and E. T. McAdams, *Innov. Tech. Biol. Med.*, **12**, 22 No. special 1 (1991).
4. F. M. Gray, *Polymer Electrolytes*, RSC Materials Monographs, J. A. Connor, Editor, The Royal Society of Chemistry, Cambridge (1997).
5. F. M. Gray and M. B. Armand, in *Handbook of Battery Materials*, J. O. Besenhard, Editor, Wiley-VCH, Weinheim (1999).
6. M. A. Ratner, P. Johansson, and D. F. Shriver, *MRS Bull.*, **XXIV**(3), 31 (2000) and references cited.
7. P. Romagnoli, G. B. Appetecchi, F. Croce, U. Heider, R. Oesten, and B. Scrosati, *Electrochem. Commun.*, **1**, 83 (1999).
8. P. Romagnoli, G. B. Appetecchi, F. Croce, L. Persi, R. Marassi, and B. Scrosati, *Electrochim. Acta*, **45**, 23 (1999).
9. D. Ostrovskii, L. M. Torell, G. B. Appetecchi, and B. Scrosati, *Solid State Ionics*, **106**, 19 (1998).
10. E. Cazzanelli, G. Mariotto, G. B. Appetecchi, F. Croce, and B. Scrosati, *Electrochim. Acta*, **40**, 2379 (1995).
11. B. Scrosati and C. A. Vincent, *MRS Bull.*, **XXIV**(3), 28 (2000).
12. C. F. Holmes, *Electrochem. Soc. Interface*, **8**(3), 32 (1999).
13. O. Escalona and E. T. McAdams, *Innov. Tech. Biol. Med.*, **16**, 58 No. special 2 (1995).