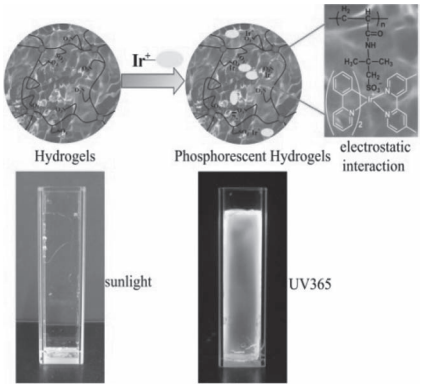
# Novel Phosphorescent Hydrogels Based on an $Ir^{III}$ Metal Complex

Zhen Li, Zhao Wei, Feng Xu, Yin Huan Li, Tian Jian Lu, Yong Mei Chen,* Gui Jiang Zhou*

Novel phosphorescent hydrogels have been explored by immobilizing an $Ir^{III}$ metal complex into the matrices of hydrogels. FTIR spectra demonstrate that the $Ir^{III}$–PNaAMPS hydrogel is achieved by irreversible incorporation of positively charged $[Ir(ppy)_2(dmbpy)]Cl$ (ppy = 2-phenylpyrine, dmbpy = 4,4′-dimethyl-2,2′-bipyridine) into negatively charged poly(2-acrylamido-2-methylpropane sulfonic acid sodium) (PNaAMPS) hydrogel via electrostatic interaction. The photoluminescent spectra indicate that the $Ir^{III}$–PNaAMPS hydrogel exhibits stable phosphorescence. In vitro cultivation of human retinal pigment epithelial cells demonstrates the cytocompatibility of the $Ir^{III}$–PNaAMPS hydrogel. This work herein represents a facile pathway for fabrication of phosphorescent hydrogels.




## 1. Introduction

As representative soft and wet biomaterials, hydrogels are shape-retentive polymeric aggregate swollen with a large amount of water in their three-dimensional (3D) networks.[1,2] The functionality of hydrogels can be achieved by material design, with examples ranging from thermoresponsive hydrogels,[3–5] electroconductive hydrogels,[6,7] magnetic hydrogels,[8,9] to luminescent hydrogels.[10–12] In particular, through endowing with luminescent properties, the hydrogels turn into a kind of luminescent biomaterials with dual functions (luminescent property and processability), which have great potential in various biomedical fields, such as bioimaging and biosensor.

Two major approaches have been developed to fabricate luminescent hydrogels. One approach is to prepare self-luminescent hydrogels directly with proper luminescent molecules as starting materials. The other approach is to prepare hybrid luminescent hydrogels by incorporation of luminescent materials into the matrices of hydrogels. Various luminescent polymers have been prepared and used as the precursor of self-luminescent hydrogels. However, it is still challenging to achieve luminescent hydrogels by molecular design.[13,14] Compared to self-luminescent hydrogels, hybrid luminescent hydrogels immobilized with luminescent materials offer several advantages, including: (I) the simple preparation process; (II) combinatorial

Y. M. Chen, Z. Li, Z. Wei, Y. H. Li, G. J. Zhou
School of Science, Department of chemistry, MOE Key Laboratory for Non-Equilibrium Synthesis and Modulation of Condensed Matter, Xi'an Jiaotong University, Xi'an 710049, P. R. China
Fax: 86-29-82668559
E-mail: chenym@mail.xjtu.edu.cn; zhougj@mail.xjtu.edu.cn
Z. Li, Z. Wei F. Xu, T. J. Lu, Y. M. Chen
Biomedical Engineering and Biomechanics Center, Xi'an Jiaotong University, Xi'an 710049, P. R. China
F. Xu
The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an 710049, P. R. China




DOI: 10.1002/marc.201200136

diversity by choosing various hydrogels and luminescent materials; (III) negligible damage to intrinsic structure of the luminescent materials, thereby maximizing their luminescent properties. The existing methods to fabricate hybrid luminescent hydrogels are mainly based on three interaction mechanisms between luminescent materials and hydrogels, that is, electrostatic interaction between poly(N-isopropyl-acrylamide) (PNIPAM)-based hydrogel and phosphorescent Au(I) complex $Na_8[Au(TPPTS)_3]$ TPPTS = tris(3,3′,3″-trisulfonatophenyl) phosphine,[11] coordination interactions between Eu(III) and the amide bond of PNIPAM or alginate hydrogel,[15,16] as well as physical encapsulation for PNIPAM or cellulose hydrogel and quantum dots.[17–19] The choice of specific interaction of combinations depends on the composition of hybrid luminescent hydrogels. In spite of the advances in luminescent hydrogels aforementioned, there is still an unmet need for a promising strategy to provide novel luminescent hydrogels through introducing outstanding luminescent materials into the matrices of hydrogels.

Iridium complexes are attracting widespread interest in many research fields for their unique optoelectronic properties.[20] For example, they are widely used in electroluminescent (EL) devices exhibiting excellent EL efficiencies for their intense phosphorescent emission and short lifetime of associated excited states.[21–26] The advantageous properties of iridium complexes have stimulated researchers to explore their applications in various areas, such as biolabeling[27] and chemosensors.[28–30] Furthermore, the cationic $Ir^{III}$ complexes have shown their potential in biolabeling of living cells.[31–33] Obviously, exploring novel application for $Ir^{III}$ complexes is a hot research area in the concerned scientific community to date. Therefore, Iridium complexes hold great potential to be promising candidate for the hybrid luminescent hydrogels. However, this has not been explored yet.

In this contribution, we prepared a novel phosphorescent hydrogel by electrostatic interaction between the positively charged $[Ir(ppy)_2(dmbpy)]Cl$ (ppy = 2-phenylpyrine, dmbpy = 4,4′-dimethyl-2,2′-bipyridine) and negatively charged poly(2-acrylamido-2-methylpropane sulfonic acid sodium) (PNaAMPS) hydrogel. The PNaAMPS hydrogel is preferred because of its proved cytocompatibility, which has been reported by us on the base of "protein-free synthetic hydrogel cell scaffold," including promoting proliferation of human umbilical vein endothelial cells, human articular chondrocytes, and mouse embryonic stem cells.[34–36]

## 2. Experimental Section

Materials, methods, analysis, and additional experimental data are supplied in the Supporting Information.

## 3. Results and Discussion

By light-induced free radical polymerization, three kinds of hydrogels, that is, anionic PNaAMPS, non-ionic poly(*N,N′*-dimethyl-acrylamide) (PDMAAm), and cationic poly(2-(methacryloyloxy) ethyltrimethylammoniumchloride) (PMETAC) hydrogels, were crosslinked by *N,N′*-methylenebis-(acrylamide) (MBAA) and initiated by 2-oxoglutaric acid (Scheme S1, Supporting Information for preparation of hydrogels). There are functional groups of sodium sulfonate ($SO_3^-$) in the pendant of PNaAMPS polymer chains, which is a strong electrolyte that endows with the negative charge of the PNaAMPS for its ionization. Similarly, the main chains of PMETAC hydrogel contain functional groups of quaternary ammonium salt ($(CH_3)_3N^+R$), which endows the hydrogel with strong positive charges. On the contrary, PDMAAm hydrogel is neutral without ionizable groups.

We first visually checked the color of the hydrogels and all three kinds of hydrogels (4 mol% crosslinking concentration) equilibrated in ion-exchanged water were transparent in swelling-state (Figure 1a). We also checked the polymeric network structure of 4 mol% PNaAMPS and 4 mol% PDMAAm using SEM (Figure S7, Supporting Information). Because of the strong electrolyte properties of PNaAMPS, the mesh size of 4 mol% PNaAMPS was obviously larger than that of 4 mol% PDMAAm. Then, we loaded iridium phosphor by immersing the three hydrogels into the aqueous solution of $[Ir(ppy)_2(dmbpy)]Cl$ ($1 \times 10^{-4}$ mol $L^{-1}$) until molecular diffusion reaches equilibrium (Figure S1, Supporting Information for preparation of iridium phosphor). The samples after this equilibration process were denoted as Eq–$Ir^{III}$–hydrogel and the corresponding residual $[Ir(ppy)_2(dmbpy)]Cl$ solution were denoted as Eq–$Ir^{III}$–solution (Figure S2, Supporting Information for preparation of phosphorescent hydrogels). When excited at 365 nm with UV lamp, these three hydrogels showed different phosphorescent responses. Compared to Eq–$Ir^{III}$–PMETAC, the Eq–$Ir^{III}$–PNaAMPS and Eq–$Ir^{III}$–PDMAAm hydrogels showed obvious phosphorescence (Figure 1b). These results demonstrated that the PNaAMPS and PDMAAm formed phosphorescent hydrogels with $[Ir(ppy)_2(dmbpy)]Cl$, while the PMETAC hydrogel did not.

To confirm the observed difference of phosphorescent phenomenon, we checked photoluminescence (PL) spectra of the three kinds of Eq–$Ir^{III}$–hydrogels. For accurate detection of the phosphorescent response of the hydrogels, the test approach was designed as follows. First, the as-prepared phosphorescent hydrogels were cut into rectangular shape (10 mm × 10 mm × 40 mm) with a self-made stainless mold to ensure 10 mm optical path. The rectangular samples were then carefully inserted into the fluorometer cell (10 mm × 10 mm × 50 mm) to

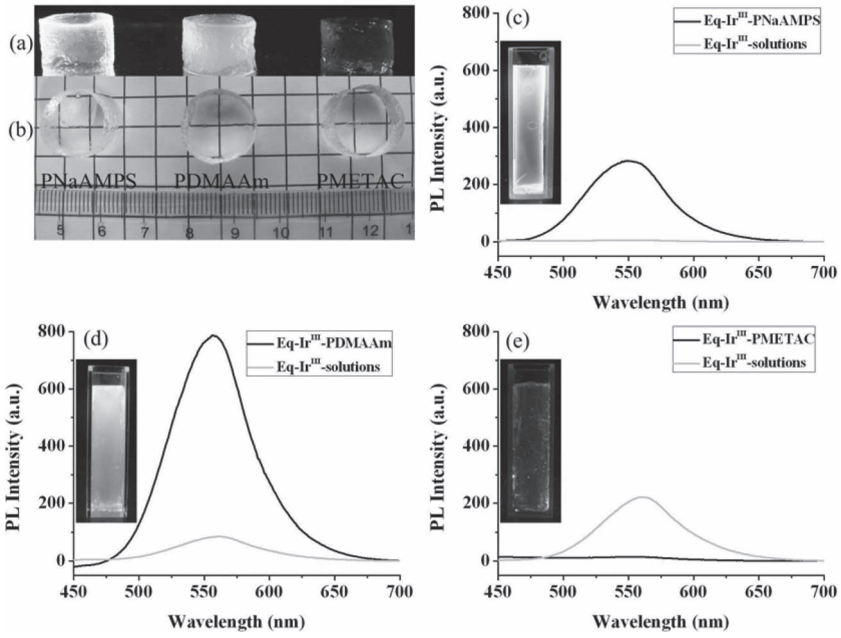



*Figure 1.* Images and PL spectra of Eq–$Ir^{III}$–hydrogels at room temperature. (a) PL images of the Eq–$Ir^{III}$–PNaAMPS, Eq–$Ir^{III}$–PDMAAm and Eq–$Ir^{III}$–PMETAC hydrogels excited at 365 nm with UV lamp. The Eq–$Ir^{III}$–PNaAMPS and Eq–$Ir^{III}$–PDMAAm hydrogels have obvious phosphorescence, while the background color of Eq–$Ir^{III}$–PMETAC hydrogels is only observed. (b) Images of PNaAMPS, PDMAAm, and PMETAC hydrogels equilibrated in ion-exchanged water under sunlight, showing their transparent property (diameter is 14.5 mm and thickness is 10 mm); (c)–(e) PL spectra excited at 365 nm of the Eq–$Ir^{III}$–PNaAMPS (c), Eq–$Ir^{III}$–PDMAAm (d) and Eq–$Ir^{III}$–PMETAC (e) compared to the control (the corresponding residual parent $[Ir(ppy)_2(dmbpy)]Cl$ solution, Eq–$Ir^{III}$–solution). For (c)–(e), the hydrogel samples were in rectangular shape (10 mm × 10 mm × 40 mm) for test. All the samples were equilibrated in $[Ir(ppy)_2(dmbpy)]Cl$ aqueous solution with concentration of $1 \times 10^{-4}$ mol $L^{-1}$ for 12 h. The average data of three samples are plotted. A color version is available in the Figure S8 (Supporting Information).

ensure that the samples were not damaged and each edges of the sample were in tight contact with the cell wall (Figure S3, Supporting Information for detailed information of test processes). After equilibrium of the hydrogels in the $[Ir(ppy)_2(dmbpy)]Cl$ solution ($1 \times 10^{-4}$ mol $L^{-1}$), the Eq–$Ir^{III}$–PNaAMPS hydrogel exhibited broad symmetrical emission with the maximal emission wavelength at 552 nm, whereas the PL intensity of the corresponding Eq–$Ir^{III}$–solution was almost undetectable (Figure 1c). The results from PL spectra illuminated that the $[Ir(ppy)_2(dmbpy)]Cl$ molecules in aqueous solution nearly completely diffused into the matrices of the PNaAMPS hydrogel. In the case of PDMAAm hydrogel, both the Eq–$Ir^{III}$–PDMAAm hydrogel and its corresponding Eq–$Ir^{III}$–solution exhibited symmetrical emission with maximal emission wavelength at 559 nm (Figure 1d). This indicated that only some of $[Ir(ppy)_2(dmbpy)]Cl$ molecules diffused into the matrices of PDMAAm hydrogel, with the other molecules remaining in the Eq–$Ir^{III}$–solution. Accordingly, the $[Ir(ppy)_2(dmbpy)]Cl$ molecules diffused into the matrices of PNaAMPS and PDMAAm hydrogels during the process of equilibrium, resulting in hybrid phosphorescent hydrogels. On the contrary, the Eq–$Ir^{III}$–PMETAC hydrogel almost showed no PL behavior, whereas the PL intensity of the corresponding Eq–$Ir^{III}$–solution was obviously higher than that of the Eq–$Ir^{III}$–PMETAC hydrogel (Figure 1e). This indicated that almost no $[Ir(ppy)_2(dmbpy)]Cl$ molecules diffused into the matrices of PMETAC hydrogel.

The results of PL spectra demonstrated that the ability of the $[Ir(ppy)_2(dmbpy)]Cl$ molecules diffused into the matrices of hydrogels is in the order of PNaAMPS>PDMAAm>PMETAC, which corresponds to anionic hydrogel, non-ionic hydrogel and cationic hydrogel. Thus, it indicated that the charge of hydrogels affects the interaction between the hydrogels and the $[Ir(ppy)_2(dmbpy)]Cl$ molecules. It can be explained as that the electrostatic attraction between the anionic PNaAMPS hydrogel and the cationic $[Ir(ppy)_2(dmbpy)]Cl$ molecules promotes the diffusion of $[Ir(ppy)_2(dmbpy)]Cl$ molecules into the matrices of hydrogels, which contributes to formation of hybrid phosphorescent hydrogel. On the contrary, the electrostatic repulsion between the cationic PMETAC hydrogel and the same charged $[Ir(ppy)_2(dmbpy)]Cl$ molecules inhibits the diffusion of $[Ir(ppy)_2(dmbpy)]Cl$ molecules into the matrices of hydrogels, which prevents the formation of hybrid phosphorescent hydrogel. In addition, we observed slightly different maximal emission wavelength of Eq–$Ir^{III}$–PNaAMPS hydrogel (552 nm) (Figure 1c) and Eq–$Ir^{III}$–solution (559 nm) (Figure 1e), resulting in yellow-green color of Eq–$Ir^{III}$–PNaAMPS hydrogel. The hypsochromic effect for the phosphorescent emission maxima of Eq–$Ir^{III}$–PNaAMPS hydrogel may be due to monomolecular phosphorescence of $[Ir(ppy)_2(dmbpy)]Cl$ molecules. The molar ratio of sodium sulfonate ($SO_3^-$) and $[Ir(ppy)_2(dmbpy)]^+$ is about 670:1 ($SO_3^-$: $Ir^+$) in Eq–$Ir^{III}$–PNaAMPS hydrogel, and the $[Ir(ppy)_2(dmbpy)]^+$ is bounded on the sodium sulfonate ($SO_3^-$) by strong electrostatic interaction. As a result, the possible interaction among the $[Ir(ppy)_2(dmbpy)]Cl$ molecules will be blocked, indicating negligible intermolecular interaction of $[Ir(ppy)_2(dmbpy)]Cl$ molecules. On the other hand, the Eq–$Ir^{III}$–PDMAAm hydrogel and Eq–$Ir^{III}$–solution had the same maximal emission (559 nm), resulting in the yellow color of Eq–$Ir^{III}$–PDMAAm hydrogel (Figure 1d).

It indicated that the free movement and probability of intermolecular interaction of the $[Ir(ppy)_2(dmbpy)]Cl$ molecules in the matrices of PDMAAm hydrogel are similar to that in water. In addition, after continuous UV excitation for 12 000 s, the PL intensity of Eq–$Ir^{III}$–PNaAMPS and $1 \times 10^{-4}$ mol $L^{-1}$ $Ir^{III}$–solutions decreased 11% and 8%, respectively (Figure S6, Supporting Information).

Considering the actual applications of Eq–$Ir^{III}$–hydrogels, it is necessary to check their stability in hydro-environment likes cell culture and native tissues. For the purpose, the Eq–$Ir^{III}$–PNaAMPS and Eq–$Ir^{III}$–PDMAAm hydrogels were immersed into ion-exchanged water. We observed an obvious phosphorescent attenuation of Eq–$Ir^{III}$–PDMAAm hydrogel after 11 d, and the phosphorescence almost completely disappeared after being balanced twice in ion-exchanged water (Figure 2b,c). RGB value of Eq–$Ir^{III}$–PDMAAm hydrogel significantly decreased (from 209, 207, 41 to 16, 18, 21) after 11 d (Figure 2e). This demonstrated that the diffusion of the $[Ir(ppy)_2(dmbpy)]Cl$ molecules into the matrices of PDMAAm hydrogel is reversible. On the other hand, after being balanced twice in ion-exchanged water, the $Ir^{III}$–PNaAMPS hydrogel still maintained phosphorescence and slightly changed from RGB (221, 237, 136) to RGB (203,229,56) after 11 d, demonstrating the stability of the Eq–$Ir^{III}$–PNaAMPS hydrogel in hydro-environment (Figure 2c,d). Furthermore, the phosphorescence can be maintained even after the Eq–$Ir^{III}$–PNaAMPS was immersed in ion-exchanged water for 9 months (Figure 3d). The results from the change of RGB value and PL intensity of Eq–$Ir^{III}$–PNaAMPS in 1 months and 9 months demonstrate the phosphorescent stability (Figure S4, S5, Supporting Information). This indicated a strong intermolecular interaction between the $[Ir(ppy)_2(dmbpy)]Cl$ molecules and PNaAMPS in Eq–$Ir^{III}$–PNaAMPS hydrogel. In order to confirm the interaction between the PNaAMPS hydrogel and the $[Ir(ppy)_2(dmbpy)]Cl$ molecules, the Fourier transform infrared (FTIR) spectra of the $[Ir(ppy)_2(dmbpy)]Cl$ powder, freeze-dried PNaAMPS and Eq–$Ir^{III}$–PNaAMPS hydrogels were checked (Figure 3a,b,c). The results showed that PNaAMPS hydrogel has the $SO_3^-$ transmittance at 1112 and 1049 $cm^{-1}$ (Figure 3b), and the Eq–$Ir^{III}$–PNaAMPS hydrogel has a new peak at 1203 $cm^{-1}$ except the peaks at the 1112 and 1049 $cm^{-1}$ (Figure 3c). The new peak at 1203 $cm^{-1}$ may correspond to the $Ir^+SO_3^-$ bond in Eq–$Ir^{III}$–PNaAMPS hydrogel. These results confirmed that there are strong electrostatic interaction between the $SO_3^-$ and $[Ir(ppy)_2(dmbpy)]^+$ in the matrices of the hydrogel (Figure 3e).

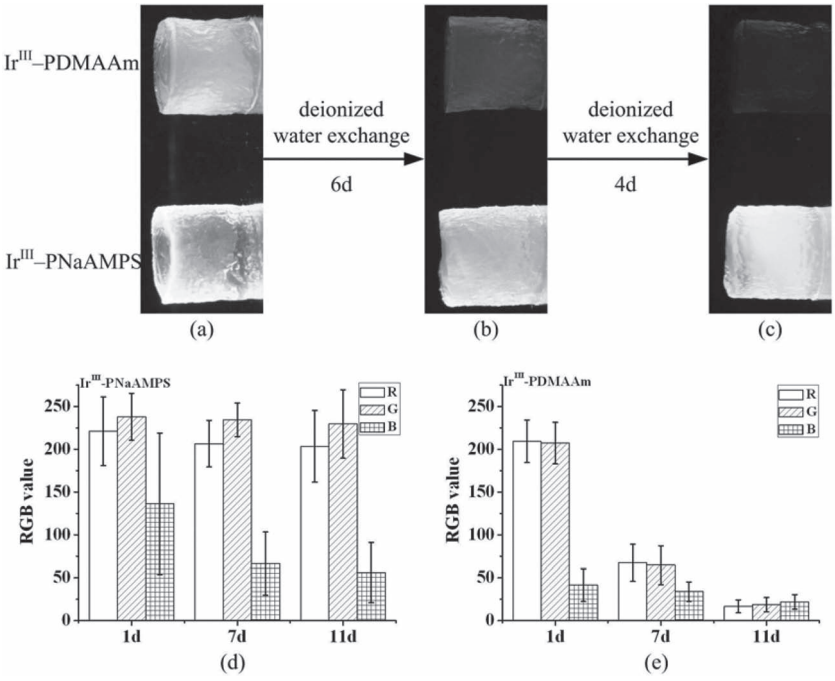



*Figure 2.* Stability of Eq–$Ir^{III}$–hydrogels in aqueous solution at room temperature. PL images of the Eq–$Ir^{III}$–PNaAMPS and Eq–$Ir^{III}$–PDMAAm hydrogels before (a) and after (b) being immersed in ion-exchanged water for 6 d, and the water of the (b) samples was changed and further immersed in the ion-exchanged water for 4 d (c). (d) and (e) were the changed scheme of RGB value of above pictures analyzed with image-proplus software. All the samples were excitated at 365 nm with UV lamp. A color version is available in the Supporting Information as Figure S9 (Supporting Information).

Cytocompatibility of the Eq–$Ir^{III}$–PNaAMPS hydrogel was also evaluated. The morphology and viability of retinal pigment epithelial (RPE) cells were assessed after 120 h of cultivation on the hydrogel. RPE cells were selected because their native substrate is transparent and soft ECM, which can be well mimicked by hydrogel in vitro.[37–39] We observed that nearly all seeding cells adhered on the hydrogel after 1 h and approximately 85% cells showed spreading morphology (fusiform or polygonal shape) after cultivation for 120 h. The spreading cells proliferated on the hydrogel with incubation time (Figure 4a). Cell viability was evaluated using a live/dead assay that stains live cells green (calcein AM) and dead cells red (ethidium homodimer). The live/dead staining showed a high level of cell survival (>98%) (Figure 4b), demonstrating the cytocompatibility of the Eq–$Ir^{III}$–PNaAMPS hydrogel. All these results indicated that the Eq–$Ir^{III}$–PNaAMPS hydrogel (equilibrated in $1 \times 10^{-5}$ mol $L^{-1}$ $[Ir(ppy)_2(dmbpy)]Cl$) support RPE cells adhesion and proliferation.

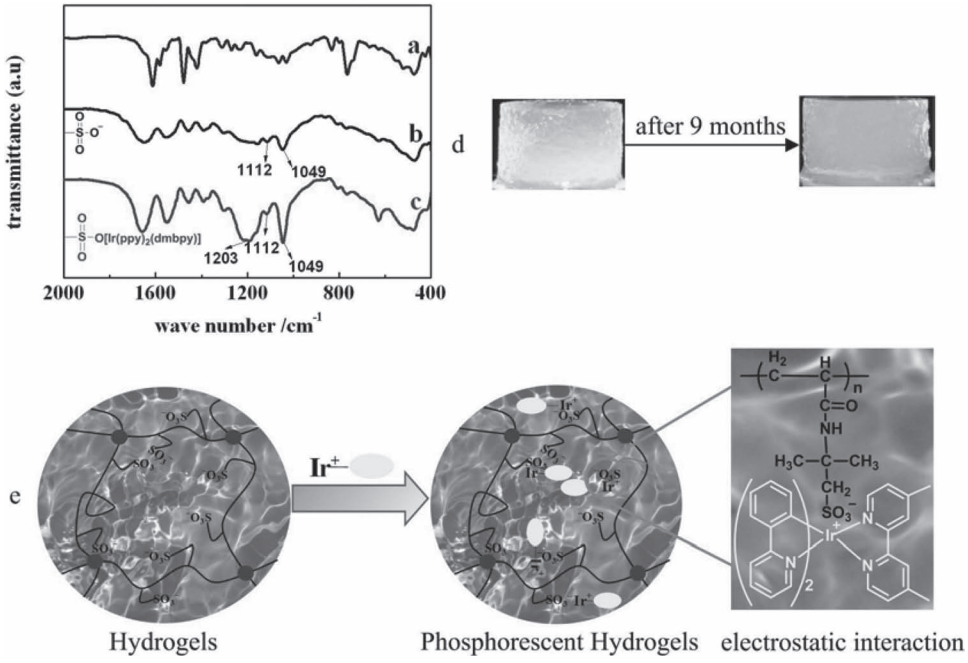



*Figure 3*. Phosphorescent stability of Eq–$Ir^{III}$–PNaAMPS hydrogel. FTIR spectra of (a) $[Ir(ppy)_2(dmbpy)]Cl$ powder and (b) freeze-dried PNaAMPS hydrogel showing the $SO_3^-$ transmittance at 1112 and 1049 $cm^{-1}$; (c) Eq–$Ir^{III}$–PNaAMPS hydrogel showing a new peak at 1203 $cm^{-1}$ corresponding to the $Ir^+SO_3^-$ bond in the hydrogel except the peaks at the 1112 and 1049 $cm^{-1}$. (d) Long-term phosphorescent stability of Eq–$Ir^{III}$–PNaAMPS hydrogels in aqueous solution at room temperature. The hydrogel was stored for 9 months and still gave phosphorescence. (e) The schematic diagram of electrostatic interaction between the PNaAMPS hydrogel and $[Ir(ppy)_2(dmbpy)]Cl$ molecules (red circle: crosslinking point, blank lines: polymer network, yellow ellipse: $[Ir(ppy)_2(dmbpy)]Cl$). A color version is available in the Supporting Information as Figure S10 (Supporting Information).

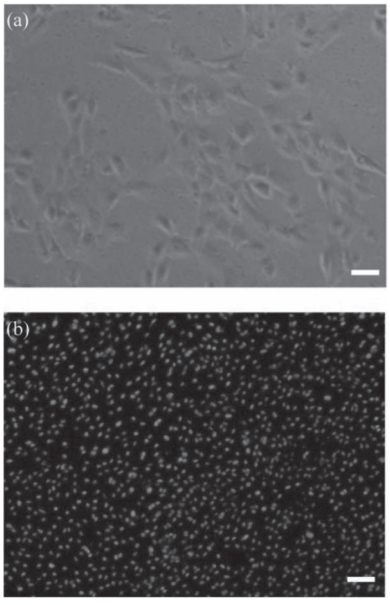



*Figure 4*. Cell morphology and live/dead assay of RPE cells cultured on 4 mol% Eq–$Ir^{III}$–PNaAMPS hydrogel ($Eq = 1 \times 10^{-5}$ mol · $L^{-1}$) scaffold for 120 h. (a) A representative image shows morphology characteristics of RPE cells (scale bar: 50 μm). (b) Live cells (green) and dead cells (red) assay showing the high level of cell survival (>98%) (scale bar: 100 μm). A color version is available in Figure S11 (Supporting Information).

## 4. Conclusion

In summary, we report a new straightforward approach for preparing novel $Ir^{III}$–PNaAMPS phosphorescent hydrogels. The $[Ir(ppy)_2(dmbpy)]Cl$ molecules were irreversibly immobilized into the matrices of the PNaAMPS hydrogels through strong electrostatic interaction between the cationic $[Ir(ppy)_2(dmbpy)]Cl$ molecules and anionic PNaAMPS hydrogels. PL spectra and FTIR spectra demonstrated outstanding phosphorescence and stability of $Ir^{III}$–PNaAMPS hydrogel, respectively. Our preliminary data showed that $Ir^{III}$–PNaAMPS supports RPE cells attachment and proliferation in vitro. Consequently, the approach provides a new direction in developing hybrid phosphorescent materials, which hold great potential in various biomedical fields as a novel biomaterial.

## Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgements: This research was supported by National Natural Science Foundation of China (Grant 51073127, 51173144, 10825210, 31050110125), the Specialized Research Fund for

the Doctoral Program of Higher Education of China (Grant 2010-0201110040), the Fundamental Research Funds for the Central Universities (2009-0109-08140018) and New Research Support Project (2009-08141001) from Xi'an Jiaotong University, P. R. China, the Major International (Regional) Joint Research Program of China (11120101002), the National 111 Project of China (B06024).

Received: February 26, 2012; Revised: April 9, 2012; Published online: May 22, 2012; DOI: 10.1002/marc.201200136

Keywords: hydrogels; $Ir^{III}$ metal complex; phosphorescence

[1] E. S. Place, J. H. George, G. K. Williams, *Chem. Soc. Rev.* **2009**, *38*, 1139.
[2] H. Geckil, F. Xu, S. J. Moon, U. Demirci, *Future Medicine: NanoMedicine* **2010**, *5*, 469.
[3] I. Frisman, Y. Shachaf, D. Seliktar, H. B. Peled, *Langmuir* **2011**, *27*, 6977.
[4] T. Mukose, T. Fujiwara, J. Nakano, I. Taniguchi, M. Miyamoto, Y. Kimura, I. Teraoka, C. W. Lee, *Macromol. Biosci.* **2004**, *4*, 361.
[5] A. A. Kavitha, N. K. Singha, *Appl. Mat. Interfaces* **2009**, *1*, 1427.
[6] A. Guiseppi-Elie, A. M. Wilson, A. R. Sujdak, K. E. Brown, *Polym. Prepr.* **1997**, *38*, 608.
[7] W. Lee, W. Lin, *J. Polym. Res.* **2002**, *9*, 23.
[8] F. Xu, C. M. Wu, V. Rengarajan, T. D. Finley, H. O. Keles, Y. Sung, B. Li, U. A. Gurkan, U. Demirci, *Adv. Mater.* **2011**, *23*, 4254.
[9] M. Zrinyi, *Colloids Surf. A: Physicochem. Eng. Aspects* **2011**, *382*, 192.
[10] G. Yilmaz, M. U. Kahveci, Y. Yagci, *Macromol. Rapid Commun.* **2011**, *32*, 1906.
[11] S. Marpu, Z. B. Hu, M. A. Omary, *Langmuir* **2010**, *26*, 15523.
[12] E. Kharlampieva, V. Kozlovskaya, O. Zavgorodnya, G. D. Lilly, Nicholas A. Kotov, V. V. Tsukruk, *Soft Matter* **2010**, *6*, 800.
[13] J. Yang, Y. Zhang, S. Gautam, L. Liuc, J. Dey, W. Chen, R. P. Mason, C. A. Serranoe, K. A. Schuge, L. P. Tang, *PNAS* **2009**, *106*, 10086.
[14] Y. J. Heo, H. Shibata, T. Okitsu, T. Kawanishi, S. Takeuchia, *PNAS* **2011**, *108*, 13399.
[15] Y. N. Jiang, X. D. Yang, C. Ma, C. Wang, H. Li, F. X. Dong, X. M. Zhai, K. Yu, Q. Lin, B. Yang, *Small* **2010**, *6*, 2673.
[16] F. Y. Liu, L. D. Carlos, R. A. S. Ferreira, J. Rocha, M. C. Gaudino, M. Robitzer, F. Quignard, *Biomacromolecules* **2008**, *9*, 1945.
[17] C. Y. Chang, J. Peng, L. N. Zhang, D. W. Pang, *J. Mater. Chem.* **2009**, *19*, 7771.
[18] X. Guo, C. F. Wang, Y. Fang, L. Chen, S. Chen, *J. Mater. Chem.* **2011**, *21*, 1124.
[19] J. Li, X. Hong, Y. Liu, D. Li, Y. W. Wang, J. H. Li, Y. B. Bai, T. J. Li, *Adv. Mater.* **2005**, *17*, 163.
[20] G. J. Zhou, W. Y. Wong, S. Suo, *J. Photochem. Photobiol. C: Photochem. Rev.* **2010**, *11*, 133.
[21] W. Y. Wong, G. J. Zhou, X. M. Yu, H. S. Kwok, Z. Y. Lin, *Adv. Funct. Mater.* **2007**, *17*, 315.
[22] L. He, J. Qiao, L. Duan, G. F. Dong, D. Q. Zhang, L. D. Wang, Y. Qiu, *Adv. Funct. Mater.* **2009**, *19*, 1.
[23] T. H. Kwon, Y. H. Oh, I. S. Shin, J. I. Hong, *Adv. Funct. Mater.* **2009**, *19*, 711.
[24] G. J. Zhou, W. Y. Wong, B. Yao, Z. Y. Xie, L. X. Wang, *Angew. Chem. Int. Ed.* **2007**, *46*, 1149.
[25] G. J. Zhou, W. Y. Wong, B. Yao, Z. Y. Xie, L. X. Wang, *Mater. Chem.* **2008**, *18*, 1799.
[26] G. J. Zhou, Q. Wang, X. Z. Wang, C. L. Ho, W. Y. Wong, D. G. Ma, L. X. Wang, Z. Y. Line, *J. Mater. Chem.* **2010**, *20*, 7472.
[27] Q. Zhao, C. H. Huan, F. Y. Li, *Chem. Soc. Rev.* **2011**, *40*, 2508.
[28] G. D. Marco, M. Lanza, A. Mamo, I. Stefio, C. D. Pietro, G. Romeo, S. Campagna, *Anal. Chem.* **1998**, *70*, 5019.
[29] M. Licini, J. A. G. Williams, *Chem. Commun.* **1999**, 1943.
[30] W. Goodall, J. A. G. Williams, *J. Chem. Soc, Dalton Trans.* **2000**, 2893.
[31] Q. Zhao, M. X. Yu, L. X. Shi, S. J. Liu, C. Y. Li, M. Shi, Z. G. Zhou, C. H. Huang, F. Y. Li, *Organometallics* **2010**, *29*, 1085.
[32] M. X. Yu, Q. Zhao, L. X. Shi, F. Y. Li, Z. G. Zhou, H. Yang, T. Yia, C. H. Huang, *Chem. Commun.* **2008**, 2115.
[33] J. S. Y. Lau, P. K. Lee, K. H. K. Tsang, C. H. C. Ng, Y. W. Lam, S. H. Cheng, K. K. W. Lo, *Inorg. Chem.* **2009**, *48*, 708.
[34] Y. M. Chen, M. Tanaka, J. P. Gong, K. Yasuda, S. Yamamoto, M. Shimomura, Y. Osada, *Biomaterials* **2007**, *28*, 1752.
[35] J. J. Yang, Y. M. Chen, J. F. Liu, T. Kurokawa, J. P. Gong, *Tissue Eng. Part A* **2010**, *16*, 2529.
[36] J. F. Liu, Y. M. Chen, J. J. Yang, T. Kurokawa, A. Kakugo, K. Yamamoto, J. P. Gong, *Tissue Eng. Part A.* **2011**, *17*, 2343.
[37] L. Lua, M. J. Yaszemskia, A. G. Mikosb, . *Biomaterials* **2001**, *22*, 3345.
[38] Y. Krishna, C. M. Sheridan, Da. L. Kent, I. Grierson, R. L. Williams, *J. Biomed. Mater. Res. A.* **2007**, *80*, 669.
[39] S. Singh, S. Woerly, B. J. Mclaughlina, *Biomaterials* **2001**, *22*, 3337.