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Artificial Chemical Systems Capable of Mimicking Some Elementary Properties of Neurons

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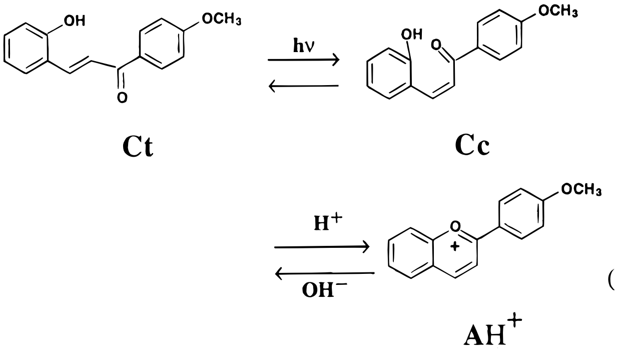
Abstract: We describe the photochemical behavior of aqueous solutions containing the $Co(CN)_6^{3-}$ complex ion and the *trans*-chalcone form **Ct** of the 4′-methoxyflavylium ion (**A**H^+). It is shown that, under the experimental conditions used, the photochemical reaction leading from **Ct** to **A**H^+ shows an *off−on−off* behavior upon excitation with a continuous light source or with successive light flashes. The described systems perform as threshold devices and as XOR (eXclusive OR) logic gates. They behave as rudimental artificial neuron-like systems in the sense that their outputs (formation of the **A**H^+ species, with a consequent change in the spectroscopic properties) are the result of an elaboration of two distinct (light) inputs by chemical reactions in solution.

Introduction

Great effort is currently devoted to mimicking the behavior of the brain using computers (Artificial Intelligence),[1,2] whereas scarce attention is paid to the design of artificial chemical systems capable of exhibiting even a minimal neuron-like behavior.[3] The neuron processes signals in a fashion that resembles the working of a tiny logic device, relying on the behavior of ions in solutions.[4,5] The neuron is quiescent unless the sum of the input signals over a period of time rises above some critical value. When such a threshold value is reached, the neuron is switched on and an output signal is generated. Recent advances in supramolecular chemistry,[6,7] and particularly the development of molecular-level systems capable of playing the role of logic gates,[8−16] begin to pave the way to research on artificial chemical networks capable of mimicking some elementary properties of neurons. In this paper we wish to report on simple (photo)chemical systems that, performing as threshold devices and as XOR (eXclusive OR) logic gates, are capable of integrating the effects of two inputs into a single output.

Results and Discussion

The basic system consists of an aqueous solution containing the *trans*-chalcone form (**Ct**, eq 1) of the 4′-methoxyflavylium



(1)

ion (**A**H^+) and the $Co(CN)_6^{3-}$ complex ion (as a potassium salt). The absorption spectra of **Ct** and $Co(CN)_6^{3-}$ are shown in Figure 1. For the present discussion, the most relevant aspects of the thermal and photochemical reactions of these two compounds, which have been studied in great detail in our laborato-

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(1) Cartwright, H. M. *Application of Artificial Inelligence in Chemistry*; Oxford University Press: New York, NY, 1993. Zupan, J.; Gasteiger, J. *Neural Networks for Chemists: An Introduction*; VCH: Weinheim, 1993.

(2) Nilson, N. J. *Artificial Intelligence: a New Synthesis*; Kaufmann Publishers: San Francisco, 1998.

(3) Amatore, C.; Thouin, L.; Warkocz, J.-S. *Chem. Eur. J.* **1999**, *5*, 456.

(4) Beale, R.; Jackson, T. *Neural Computing: An Introduction*; Adam Hilger: Bristol, 1990.

(5) Hubel, D. H. *Eye, Brain and Vision*; Scientific American Library: New York, 1995.

(6) Lehn, J.-M. *Supramolecular Chemistry. Concepts and Perspectives*; VCH: Weinheim, 1995.

(7) Atwood, J. L.; Davies, J. E. D.; MacNicol, D. D.; Vötgle, F. Eds. *Comprehensive Supramolecular Chemistry*; Pergamon Press: Oxford, 1996; Vols. 1−10.

(8) **)** De Silva, A. P.; Guranatne, H. Q. N.; McCoy, C. P. A. *Nature* **1993**, *364*, 42.

(9) Rouvray, D. *Chem. Br.* **1995**, *31*, 544.

(10) Credi, A.; Balzani, V.; Langford, S. J.; Stoddart, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 2679.

(11) Pina, F.; Roque, A.; Melo, M. J.; Maestri, M.; Belladelli, L.; Balzani, V. *Chem. Eur. J.* **1998**, *4*, 1184.

(12) Rouvray, D. *Chem. Br.* **1998**, *34*, 26.

(13) Gosztola, D.; Niemczyk, M. P.; Wasielewski, M. *J. Am. Chem. Soc.* **1998**, *120*, 5118.

(14) Faulkner, S.; Parker, D.; Williams, J. A. G. In *Supramolecular Chemistry: Where It Is and Where It Is Going*; Ungaro R., Dalcanale, E., Eds.; Nato ASI Series; Kluwer Academic Publishers: Dordrecht, 1999.

(15) Collier, C. P.; Wong, E. W.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F.; Kuekes, P. J.; Williams, R. S.; Heath, J. R. *Science* **1999**, *285*, 391.

(16) De Silva, A. P.; Dixon, I. M.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Maxwell, P. R. S.; Rice, T. E. *J. Am. Chem. Soc.* **1999**, *121*, 1393.

10.1021/ja000190d CCC: $19.00

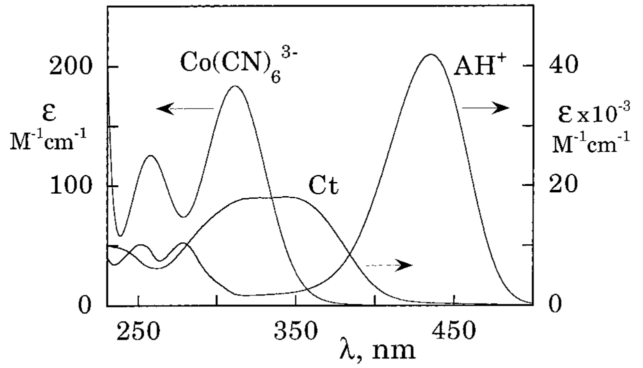

Figure 1. Absorption spectra of the compounds **Ct**, **AH**$^+$, and $Co(CN)_6^{3-}$ in aqueous solution. The structure formulas of **Ct** and **AH**$^+$ are shown in eq 1.

ries,[17,18] are as follows. Excitation by 365 nm light of **Ct**, which is the thermodynamically stable form of the flavilyium species in the pH range 3−7, causes a trans → cis photoisomerization reaction, eq 1 (quantum yield = 0.04).[17]

If the solution is sufficiently acid (pH <4), the **Cc** isomer is rapidly protonated with conversion to the 4′-methoxyflavylium ion **AH**$^+$, which is kinetically stable under such pH conditions and exhibits an intense absorption band with maximum at 434 nm (Figure 1) and an emission band with maximum at 530 nm. At higher pH values, however, protonation does not occur and the **Cc** photoproduct is back converted to **Ct**. As far as $Co(CN)_6^{3-}$ is concerned, excitation by 254 or 365 nm light in acid or neutral aqueous solution causes the dissociation of a CN^- ligand from the metal coordination sphere (quantum yield = 0.31), with a consequent increase in pH:[18]

$$\mathrm{Co(CN)_6}^{3-} + \mathrm{H_3O^+} + h\nu \rightarrow \mathrm{Co(CN)_5(H_2O)}^{2-} + \mathrm{HCN} \quad (2)$$

Continuous Irradiation. When an acid solution (pH 3.6) containing 2.5×10^{-5} M **Ct** and 2.0×10^{-2} M $Co(CN)_6^{3-}$ is irradiated at 365 nm, most of the incident light is absorbed by **Ct** (Figure 1), which undergoes photoisomerization to **Cc**. Since the pH of the solution is sufficiently acid, **Cc** is rapidly protonated (eq 1), with the consequent appearance of the absorption band with maximum at 434 nm (Figure 2) and of the emission band with maximum at 530 nm characteristic of the **AH**$^+$ species.[17] On continuing irradiation, it can be observed that the absorption (Figures 2 and 3) and emission bands increase in intensity, reach a maximum value, and then decrease up to complete disappearance. These results show that **AH**$^+$ first forms and then disappears with increasing irradiation time.

The reason for the *off*−*on*−*off* behavior[19] of **AH**$^+$ under continuous light excitation is related to the effect of reaction 2 on reaction 1. As **Ct** is consumed by reaction 1 with formation of **AH**$^+$, an increasing fraction of the incident light is absorbed by $Co(CN)_6^{3-}$, which undergoes reaction 2. Such a photoreaction causes an increase in the pH of the solution. This not only prevents further formation of **AH**$^+$, which would imply protonation of the **Cc** molecules that continue to be formed by light excitation of **Ct**, but also causes the back reaction to **Cc** (and, then, to **Ct**) of the previously formed **AH**$^+$ molecules. Clearly, the examined solution performs like a threshold device as far as the input (light)/output (spectroscopic properties of **AH**$^+$) relationship is concerned.

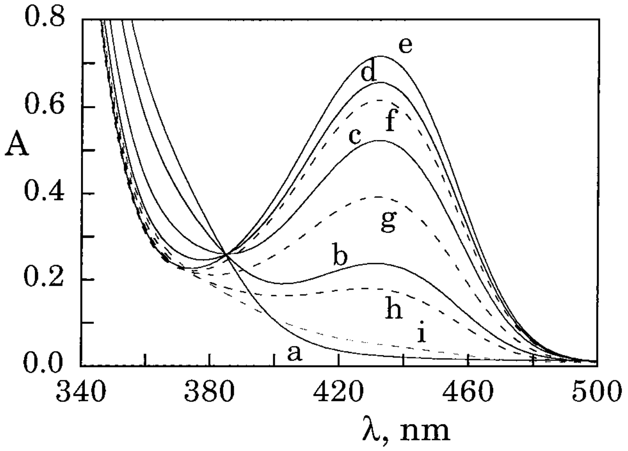

Figure 2. Spectral changes observed for an aqueous solution containing 2.5×10^{-5} M **Ct** and 2.0×10^{-2} M $Co(CN)_6^{3-}$ on irradiation with light of 365 nm. The curves correspond to the following irradiation times (in minutes): (a) 0; (b) 1.5, (c) 4.5, (d) 7.5, (e) 12.5, (f) 20, (g) 27.5, (h) 32.5, and (i) 37.5. The reason the isosbestic point at 385 nm is not maintained when **AH**$^+$ disappears (curves f−i) is that the back conversion of **Cc** to **Ct** (eq 1) is relatively slow and needs longer time periods to be completed.

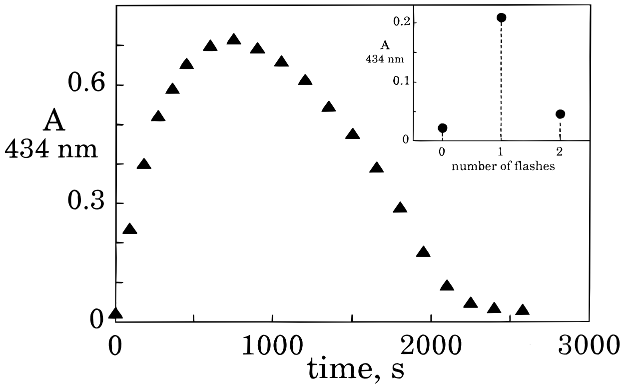

Figure 3. Changes in absorbance at 434 nm with increasing irradiation time upon continuous irradiation with 365 nm light (see Figure 2). The inset shows the absorption changes at 434 nm caused by two successive flash inputs of 355 nm light on the same solution.

Pulsed Irradiation. Instead of a continuous light source, pulsed (flash) irradiation can be used. The results obtained with two equally intense flashes are displayed in the inset of Figure 3. Under the input of only one flash, a strong change in absorbance at 434 nm is observed, due to the formation of **AH**$^+$. After two flashes, however, the change in absorbance practically disappears. In other words, an output (434 nm absorption) can be obtained only when *either* input 1 (flash I) *or* input 2 (flash II) is used, whereas there is no output under the action of *none* or *both* inputs. This shows that the above-described system (Figure 4a) behaves according to an XOR (eXclusive OR) logic, under control of an intrinsic threshold mechanism. It is noteworthy that the input and output signals have the same nature (light).

Second Generation Systems. Further elaboration of the above concept leads to the design of more complex, but also more flexible, artificial chemical networks. That schematized in Figure 4b reminds one of the scheme describing a minimal array of perceptrons, the artificial intelligence units used to

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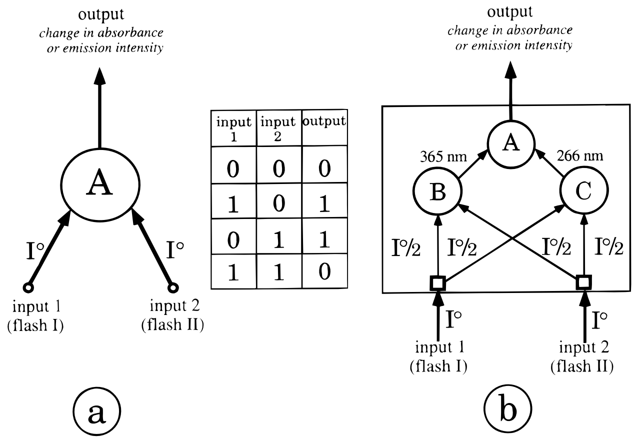
[17] Pina, F.; Melo, M. J.; Maestri, M.; Ballardini, R.; Balzani, V. *J. Am. Chem. Soc.* **1997**, *119*, 5556.

[18] Moggi, L.; Bolletta, F.; Balzani, V.; Scandola, F. *J. Inorg. Nucl. Chem.* **1966**, *28*, 2589.

[19] For systems showing *off*−*on*−*off* behavior, see: (a) De Silva, A. P.; Guranatne, H. Q. N.; McCoy, C. P. A. *J. Chem. Soc., Chem. Commun.* **1996**, 2399. (b) De Silva, S. A.; Zavaleta, A.; Baron, D. E.; Allam, O.; Isidor, I. V.; Kashimura, N.; Percapio, J. M. *Tetrahedron Lett.* **1997**, *38*, 2237. (c) Fabbrizzi, L.; Licchelli, M.; Poggi, A.; Taglietti, A. *Eur. J. Inorg. Chem.* **1999**, 35.



input 1	input 2	output
0	0	0
1	0	1
0	1	1
1	1	0

Figure 4. Schematic representation of the two described systems and truth table of the eXclusive OR (XOR) logic behavior. (a) Inputs 1 and 2 are two equally intense pulsed light beams (355 nm, third harmonic of a Neodymium laser) generated by flash sources (flash I and flash II). The reaction cell A contains 2.5×10^{-5} M **Ct** and 2.0×10^{-2} M $Co(CN)_6^{3-}$ in aqueous solution at pH 3.6. The output is the absorption ($\lambda_{max} = 434$ nm) or the emission ($\lambda_{max} = 530$ nm) bands of the **A**H$^+$ species formed in the reaction cell. The results obtained are illustrated in the inset of Figure 3. (b) Inputs 1 and 2 are two equally intense pulsed light beams at 266 nm (fourth harmonic of a Neodymium laser) generated by flash sources (flash I and flash II). Cell A contains an aqueous solution of **Ct** and $Co(CN)_6^{3-}$. Cell B contains a solution of a fluorophore (e.g., naphthalene) which emits around 365 nm, and cell C contains a solution that absorbs, and can be bleached by, 266 nm light (e.g., a $Co(CN)_6^{3-}$ aqueous solution). The concentrations of the solutions should be adjusted on the basis of the geometrical setup of the system and the intensities of the light pulses. The output is the absorption ($\lambda_{max} = 434$ nm) or the emission ($\lambda_{max} = 530$ nm) bands of the **A**H$^+$ species formed in cell A.

mimic the behavior of neurons.[1] In such a system, inputs 1 and 2 are two equally intense (I^o) pulses of UV light at 266 nm emitted by two independent light sources (flash I and flash II). Each light pulse is subdivided in two equally intense ($I^o/2$) beams. One beam of each pulse is sent through a cell B containing a solution of a fluorophore (e.g., naphthalene), in which absorption of 266 nm light causes an emission around 365 nm. Such an emitted light is used to excite an appropriate **Ct**-$Co(CN)_6^{3-}$ aqueous solution (vide supra) contained in cell A. The other beam of each pulse, before arriving at cell A, has to cross cell C containing a solution that absorbs, and can be bleached by, 266 nm light (e.g., a $Co(CN)_6^{3-}$ aqueous solution). In such a system, when only one input (i.e., one of the two flashes) is used, a beam of 266 nm light is completely absorbed by cell C, whereas the other beam excites the fluorophore contained in cell B. This leads to the generation of 365 nm light that, absorbed by **Ct** contained in cell A (Figure 1), causes its conversion into **A**H$^+$ (eq 1), with a consequent increase in absorbance at 434 nm and emission at 530 nm. When both flashes are consecutively fired, the intensity of the 365 nm light incident on A, originating from B, doubles, which would imply a consequent doubling of the amount of **Ct** converted into **A**H$^+$. At the same time in cell C the first pulse bleaches the $Co(CN)_6^{3-}$ solution, so that the second pulse of the 266 nm light is transmitted to cell A. This causes the photoreaction of $Co(CN)_6^{3-}$ (see the absorption spectrum of $Co(CN)_6^{3-}$ in Figure 1 and its photoreaction in eq 2), with a consequent increase in pH and back conversion of the previously formed **A**H$^+$ molecules to **Cc** and then to **Ct**. Clearly, also this system would perform as a threshold device and as a XOR logic gate (Figure 4). Furthermore, in this case the input/output relationship may be changed at will by changing the "weights" of the connecting signals (e.g., the splitting ratio of each incident light pulse or the composition of the solutions contained in the cells).

Conclusions

We would like to point out that the described systems are based on simple chemical compounds and well-documented photochemical and photophysical processes taking place in aqueous solution. What is new are the integration of the effects of two inputs into a single output and the conceptual interpretation of the results obtained. The systems behave as rudimentary artificial neurons in the sense that their outputs (formation of the **A**H$^+$ species, with a consequent change in the spectroscopic properties) are the result of an elaboration of two distinct (light) inputs by chemical reactions in solution. More complex neuron-like chemical networks can be designed along these lines. These studies could also contribute to the development of the idea of artificial molecular-based computers.[12,20,21]

Experimental Section

$K_3Co(CN)_6$ and 4′-methoxyflavylium perchlorate were available from previous investigations.[17,18] Absorption and emission spectra were recorded with Perkin-Elmer Lambda 16 and LS 50 instruments. The 365 nm light for continuous irradiation was obtained from a medium-pressure mercury lamp filtered by an interference filter. The incident light intensity (4.6×10^{-7} N $h\nu$/min) on the reaction cell (3 mL) was measured with a ferrioxalate actinometer.[22] Flash inputs of 355 nm light were obtained from the third harmonic of a Neodymium YAG laser (Continuum, Surelite I-10). The irradiated volume (0.3 mL) was adapted to the intensity of the laser flash (ca. 3×10^{-7} N $h\nu$/pulse).

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(20) Ball, P.; Garvin, L. *Nature* **1992**, *55*, 761.
(21) Bradley, D. *Science* **1993**, *259*, 890.
(22) Hatchard, C. G.; Parker, C. A. *Proc. R. Soc. London, Ser. A* **1956**, *235*, 518.