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Molecular switches based on cyanoferrate complexes

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Contents

Abstract

A new system able to play the role of a molecular switch has been characterised. The system consists of the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ complexes in equilibrium. The constituent complexes differ considerably in electronic absorption (especially in the visible region) and undergo photochemical reactions proceeding in distinct spectral ranges and yielding different products. The equilibrium can be shifted by several physical and chemical stimuli changing thereby absorption and/or modifying the photochemical behaviour of the system. To the stimuli belong: pH, thiol concentration, ion strength, nature and concentration of cations, temperature and pressure. All these features make the system suitable for switching purposes and for different kinds of signal processing in digital, analogue and integrating circuits. As the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system photochemically produces NO-donors and/or nitric oxide, its phototherapeutic application is considered.

Keywords: Nitroprusside; Pentacyanoferrates(II); Thiolate; Mercaptosuccinate; Nitric oxide; NO-donors; Molecular switch

1. Introduction

In most cases, molecular devices consist of molecular components performing desired actions, and these components are all usually bound together to form a supramolecular assembly. Building blocks of supramolecular devices usually perform actions like light absorption and/or emission, energy transfer and/or electron transfer, isomerisation and/or other chemical reactivity [1–7]. In most cases the systems able to perform a desired action are extremely complex supramolecular systems. Moreover, it is very difficult to build systems executing more complex functions, like signal computing. Looking for a simple and effective system working at the molecular level we turned our attention to the cyanide complexes, which are recently used to construct multi-dimensional cyanide-bridged assemblies with interesting magnetic and many other properties [8–15]. Moreover, the unique and versatile properties of the cyano ligands make the chemistry and photochemistry of their complexes very rich.

The best example of this behaviour is presented by the cyanoferrates(II). First of all, in contrast to most other Fe(II) complexes, cyanoferrates(II) are photochemically active. Moreover, depending on the irradiation energy and the nature of the co-ligand, they undergo photosubstitution, and/or diverse photoredox reactions. In the

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case of the $[Fe(II)(CN)_5L]^{n-}$ complexes, a metal centered (MC) excited state leads to substitution of either the L or CN^- ligand, depending on the π-bonding properties of the L ligand [16,17]. Photooxidation mode, following MLCT, LLCT or even MC+LC (ligand centered) transitions, can be either outersphere (for $L = CN^-$ or CO) or innersphere, accompanied by substitution (in the case of $L = NO^+$) [16,17]. Finally, the same complex, $[Fe(CN)_5NO]^{2-}$, can undergo both photooxidation and photoreduction, depending on the reactive excited state [16,17].

Considering the prospective use of cyanoferrates as the basis of a molecular switch, the crucial role of their thermal reactivity and flexible photochemical behaviour must be taken into account. From this point of view the best object for such a study is nitrosylpentacyanoferrate(2−), commonly called nitroprusside, not only due to its rich photochemistry but also because of its susceptibility to undergo a nucleophilic attack. Moreover, the $[Fe(CN)_5NO]^{2-}$ complex belongs to a group of compounds, whose effectiveness in nitric oxide generation is of biological importance [17–20]. The interest in the NO-donors and the controlled delivery of NO to the selected tissues has increased recently because a new role of nitric oxide in photodynamic therapy (PDT) has been discovered [21–25]. Nitric oxide released in leukemic cells among others enhances their radiation sensitivity, stimulates the antitumour immune response and can even be toxic towards some of these cells [24–29]. Construction of a system playing the role of molecular device able to control NO delivery seems to be of special value.

2. Properties and photochemistry of the $[Fe(CN)_5N(O)SR]^{3-}$ complexes

Amongst the NO-donors of biomedical importance, interest is focused on metal nitrosyl complexes and S-nitrosothiols due to the significant enhancement of their NO-release upon irradiation. Enhanced effectiveness and/or versatility could be expected in the case of the simultaneous action of both the NO-donors. Fortunately, nitroprusside readily undergoes a nucleophilic attack at the N(NO) atom, and thus reacts with thiolate ions (containing deprotonated S-atom, for sake of simplicity represented by the symbol with one negative charge, RS^-) forming complex with the nitrosothiolato ligand:

$$[Fe(CN)_5NO]^{2-} + RS^- \rightleftarrows [Fe(CN)_5N(O)SR]^{3-} \quad (1)$$

Unfortunately, in most cases the reaction product is thermally unstable and in redox decomposition yields disulphide and nitrosylpentacyanoferrate(3−) [17,30–37].

$$[Fe(CN)_5N(O)SR]^{3-} \rightarrow [Fe(CN)_5NO]^{3-} + 1/2RSSR \quad (2)$$

$$[Fe(CN)_5N(O)SR]^{3-} + RS^- \rightarrow [Fe(CN)_5NO]^{3-} + RSSR^{\bullet -} \quad (3)$$

Fortunately, the stability of the nitrosothiolate complex depends strongly on the nature of the thiolate: Insertion of an electronegative substituent into the thiol moiety considerably increases the complex stability and when, for instance, thiol has two carboxylic groups, as in $RS^- =$ mercaptosuccinate, the complex is thermally stable enough for the photochemical study [36].

Considering the nitroprusside and its mercaptosuccinate derivative with respect to their prospective use as NO-donors two properties are of crucial importance: action spectrum and photochemical behaviour. Concerning the former (Fig. 1), NO-donation by $[Fe(CN)_5NO]^{2-}$ can be switched practically by light of wavelength not longer than 500 nm, whereas $[Fe(CN)_5N(O)SR]^{3-}$ photosensitivity reaches as far as 700 nm, i.e. fairly near the phototherapeutic window [30,38].

The photochemistry of nitroprusside is well documented. Exposure to UV-A ($\lambda > 315$ nm) causes photooxidation–substitution reaction [16,39–44]

$$[Fe(CN)_5NO]^{2-} + H_2O \xrightarrow{h\nu} [Fe(III)(CN)_5H_2O]^{2-} + NO^{\bullet} \quad (4)$$

whereas irradiation within UV-B ($\lambda \leq 315$ nm) induces photoreduction yielding $[Fe(CN)_5NO]^{3-}$ [16,39,40]. Thus, to produce NO the radiation wavelength should be greater than ~315 nm, but increase in irradiation wavelength decreases sharply the quantum yield of the reaction (4) from 0.33 at 313 nm to 0.006 at 546 nm [30]. The need to use the UV-A radiation to trigger the NO photodelivery makes the system not very useful for phototherapy purposes.

As the $[Fe(CN)_5N(O)SR]^{3-}$ synthesis from $[Fe(CN)_5NO]^{2-}$ and thiolate anion is a reversible reaction (cf. Eq. 1), nitroprusside is the inherent constituent of the system and thus its interference had to be taken into account in a photochemical study of the nitrosothiolate complex. The main effects come from the photochemical reactivity of $[Fe(CN)_5NO]^{2-}$ and from its very fast reactions with RS^- (Eq. 1). To avoid the former effect, the photochemistry of the nitrosothiolate complex is carried out within the radiation region not absorbed by the $[Fe(CN)_5NO]^{2-}$ ion ($\lambda > 500$ nm). The excitation involves the MLCT transition, which is effective in population of the antibonding orbital, localised at the RSNO ligand. In consequence, two primary processes are recorded: one following the N–S bond cleavage within the nitrosothiolato ligand (Eq. 5) and the other consisting of electron transfer and

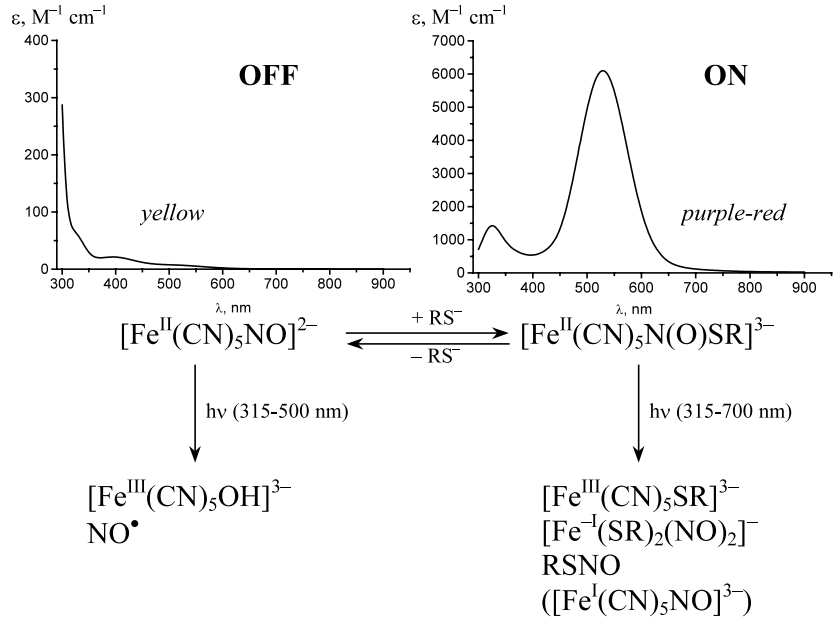
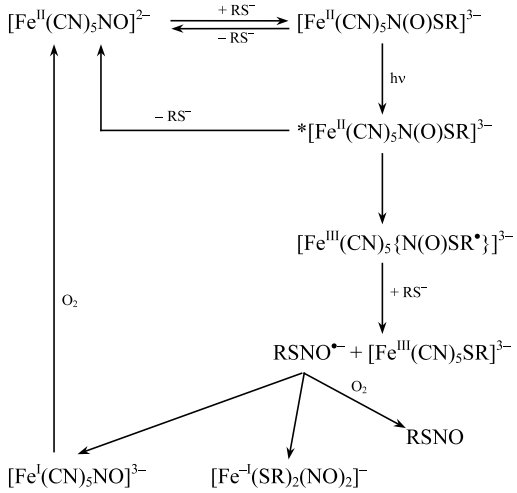


Fig. 1. Versatile optical and photochemical properties of the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system.



Scheme 1. Photochemical and secondary thermal reactions proceeding in alkaline (pH 10) solution containing $[Fe(CN)_5N(O)SR]^{3-}$, $[Fe(CN)_5NO]^{2-}$ and RS^- = mercaptosuccinate, upon excitation of $[Fe(CN)_5N(O)SR]^{3-}$ within 500–700 nm.

substitution (Eq. 6, cf. also Scheme 1) [17,30,36,45].

$$[Fe(CN)_5N(O)SR]^{3-} \xrightarrow{h\nu} [Fe(II)(CN)_5NO]^{2-} + RS^- \quad (5)$$

$$[Fe(CN)_5N(O)SR]^{3-} + RS^- \xrightarrow{h\nu} [Fe(III)(CN)_5SR]^{3-} + RSNO^{\bullet -} \quad (6)$$

The production of an additional amount of nitroprusside in the photodissociation (Eq. 5) upsets the equilibrium (Eq. 1), which is restored in fast chemical relaxation (relaxation time τ of the order of milliseconds). Among the products of the second photoreaction (Eq. 6) the $[Fe(III)(CN)_5SR]^{3-}$ complex is relatively stable ($\tau_{1/2} > 650$ s), whereas the $RSNO^{\bullet -}$ radical ($\tau_{1/2} = 4$ μs) is responsible for most of the secondary thermal reactions in the system [38]. Among others, the oxidative decay of the $RSNO^{\bullet -}$ radicals is responsible for the reduction of the iron complexes. Detailed reactions are dependent strongly on the system components: in the presence of excess thiol, the main pathway of $RSNO^{\bullet -}$ decay is reaction with the nitrosothiolate complex:

$$[Fe(II)(CN)_5N(O)SR]^{3-} + RSNO^{\bullet -} + 2RS^- \rightarrow [Fe(-I)(SR)_2(NO)_2]^- + RSSR + 5CN^- \quad (7)$$

when nitroprusside is in excess, the radical oxidation yields nitrosothiol:

$$[Fe(II)(CN)_5NO]^{2-} + RSNO^{\bullet -} \rightarrow [Fe(I)(CN)_5NO]^{3-} + RSNO \quad (8)$$

whereas in the presence of oxygen, the nitrosothiol production is accompanied by generation of the O_2^- radicals:

$$RSNO^{\bullet -} + O_2 \rightarrow RSNO + O_2^{\bullet -} \quad (9)$$

In the presence of oxygen, nitroprusside is also regenerated from the $[Fe(I)(CN)_5(NO)]^{3-}$ complex.

The sequence of the primary and secondary thermal processes (Scheme 1), yields $[Fe(III)(CN)_5SR]^{3-}$, $[Fe(I)(CN)_5NO]^{3-}$, $[Fe(-I)(SR)_2(NO)_2]^-$, RSNO and RSSR as the final products. Amongst the products, $[Fe(-I)(SR)_2(NO)_2]^-$ and RSNO are known as efficient NO-donors [18,25,26], whereas $[Fe(I)(CN)_5NO]^{3-}$ is unable to release NO [20], although some authors considered this compound as responsible for the fast nitroprusside metabolism [46]. Production of $[Fe(I)(CN)_5NO]^{3-}$ can be minimised by the presence

of oxygen and an excess of thiolate. Under such conditions the total concentration of the NO-donors increases linearly with irradiation time within 500–700 nm [38], demonstrating that the nitrosation capacity and thus therapeutic power of the system is adaptable to the phototherapy targets.

3. Properties of the $[Fe(CN)_5NO]^{2-}$ – $[Fe(CN)_5N(O)SR]^{3-}$ system

Due to the fast reaction between nitroprusside and thiolate (Eq. 1) [36,38,47], the nitrosation agents are produced at the expense of nitroprusside even though the $[Fe(CN)_5N(O)SR]^{3-}$ complex absorbs light and undergoes the photooxidation–substitution reaction. Although, the $[Fe(CN)_5N(O)SR]^{3-}$ photoreaction is in reality the photoassisted reaction of nitroprusside with mercaptosuccinate photoactivator [38], the photoproducts are different from those generated in neat $[Fe(CN)_5NO]^{2-}$ solutions [30,38]. The different photochemical behaviour, differences in the absorption spectra and photoreactivity ranges for the complexes involved in equilibrium created the basis of the system to play a role of a molecular switch (Fig. 1).

In order to find a practical application for the system, the parameters controlling the equilibrium (Eq. 1) and their influence on photoreactivity had to be recognised. To the most important physical and chemical stimuli shifting the equilibrium and thus modifying the photochemical behaviour of the system belong: pH, thiol concentration, ion strength, nature and concentration of cations, temperature and pressure.

The effect of pH is very simple: it consists of removing the nucleophile, i.e. the thiolate anions by their protonation at low pH, and thus shifts the equilibrium (1) to the left and vice versa, when pH value is increased (Fig. 2). Changes in the thiolate concentration have a similar effect [36].

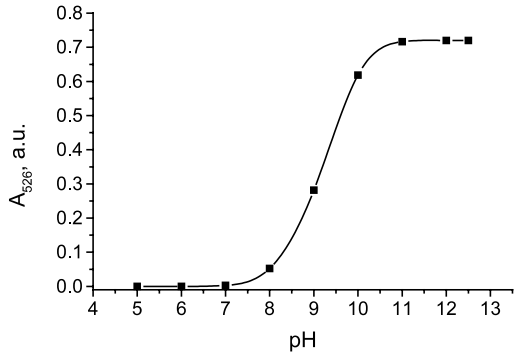


Fig. 2. Influence of pH on the equilibrium (1) shift as followed by absorption changes at 526 nm. Experimental conditions: initial concentrations: $[Fe(CN)_5N(O)SR]^{3-}$ 1.0 mM, mercaptosuccinate 5.0 mM, KCl 0.5 M in 0.2 M Tris–HCl buffer.

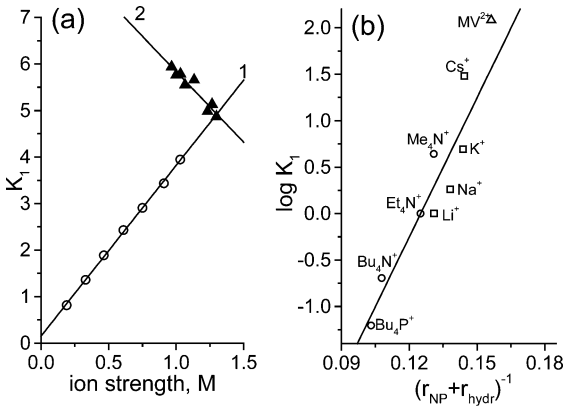


Fig. 3. Dependence of the equilibrium (1) constant, K_1, on: (a) ionic strength made by a variable cation (Na^+) concentration (line 1) and by anion changes at constant cation (K^+) concentration (line 2); (b) reciprocal sum of nitroprusside and hydrated radii of different cations (adapted from [36]). Experimental conditions: initial concentrations: $[Fe(CN)_5N(O)SR]^{3-}$ 1.0 mM, mercaptosuccinate 5.0 mM, pH 10 (carbonate–borate buffer), $T = 298$ K.

Much more sophisticated are the influences of cations and ion strength. Increasing ion strength at constant cation concentration shifts the equilibrium to the left [36] (Fig. 3a). This effect may have several explanations: Increasing ion strength at constant cation concentration can be achieved only by increase in the anion charge (e.g. substitute SO_4^{2-} for Cl^-). Anions with the higher charge can compete effectively with nitroprusside in binding cations. Moreover, increasing ion strength, according to Debye–Hückel equation, decreases the mean activity coefficients of the ionic reactants. Finally, the ionisation constant of the –SH group of mercaptosuccinic acid is known to depend on the anions present in solution [48].

The opposite effect is observed when ion strength is increased by increased cation concentration: Then, as can be expected for a anion–anion reaction [49–54], the equilibrium constant for the reaction (1) increases linearly with increasing cation concentration [36] (Fig. 3a). The magnitude of the shift, however, depends strongly on the nature of the cation. For several alkali metal and tetraalkylammonium cations, simple electrostatic interaction seems to play a crucial role. Bulky tetraalkylammonium and tetraalkylphosphonium cations disfavour formation of the $[Fe(CN)_5N(O)SR]^{3-}$ complex, while smaller cations tend to stabilise it. The dependence of ln K versus reciprocal sum of hydrated radii of nitroprusside and the cations follows linear trend (Fig. 3b). Some nonlinearities observed for the cation effect originate from some specific interactions, like hydrogen bonding, redox potential and polarisability of the cation as well as medium viscosity [36,55].

Equilibrium (1) is very sensitive to temperature and pressure. A solution containing $[Fe(CN)_5NO]^{2-}$ and $[Fe(CN)_5N(O)SR]^{3-}$ complexes in equilibrium exhibits

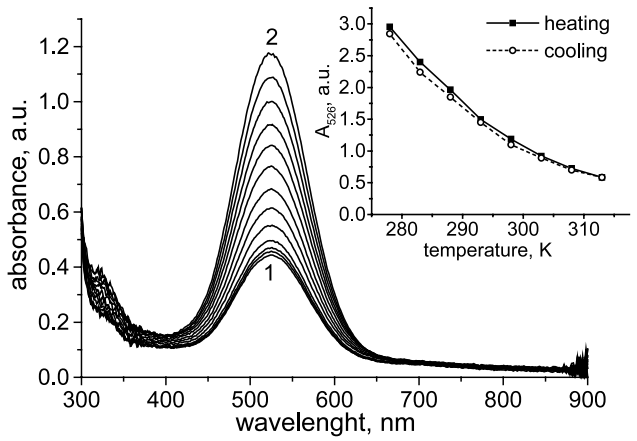


Fig. 4. Effect of pressure on the equilibrium (1) shift, as shown by changes in the UV–vis spectra of the system containing nitroprusside (1 mM) and mercaptosucinate (5 mM) at 288 K and pressure (MPa): 0.1 (line 1), 5, 10, 20, 40, 60, 80, 100, 120, 140, 160, 180, 200 (line 2). Insert: effect of temperature on the same system under ambient pressure, followed at λ_{max} 526 nm. Experimental conditions: pH 10 (carbonate–borate buffer), $[K^+] = 0.2$ M.

strong increase in absorption with decrease in temperature or increase in pressure (Fig. 4). The effect is totally reversible: increasing temperature or decreasing pressure returns the original equilibrium position [56,57]. Moreover, the magnitude of these changes depends on the nature of the cation, as ΔH, ΔS and ΔV of the reaction (1) were found to depend strongly on the cations [56,57].

All these parameters can be used to manipulate the equilibrium and hence to change optical properties (absorption) and the photochemical behaviour of the system containing $[Fe(CN)_5NO]^{2-}$ and $[Fe(CN)_5N(O)SR]^{3-}$ in equilibrium (1). This can be switched on and off reversibly by any of the above mentioned physical and chemical stimuli.

All these features make the system a very good model for switches at the molecular level. The complex molecules are very small as compared with supramolecular assemblies but the system is very suitable for switching purposes and for different kinds of signal processing, both in analogue and in digital systems. The analogue approach requires only selection of suitable input parameters and steering stimuli from all accessible quantities influencing the system (vide supra). In analogue mode, several units for signal processing can be designed.

4. Reversible switching systems

The simplest device the system can mimic is a switch. The optical properties and photochemical behaviour of the system depend on the state of equilibrium (cf. Fig. 1). In the OFF state (equilibrium shifted to the left) the solution is yellow and UV-A irradiation generates NO, whereas visible irradiation is practically not active. Thus in the system containing nitroprusside and thiol the $[Fe(CN)_5N(O)SR]^{3-}$ complex is not formed, i.e. the equilibrium (1) is shifted completely to the left. Adequate application of any of the switching stimuli (pH, cations etc.) shifts the equilibrium (1) to the right. This process can also be described as a transition of the system from the OFF to the ON state. The states can easily be distinguished because they demonstrate different optical properties and photoreactivity: a system in the OFF state absorbs mostly UV light and generates NO upon irradiation, while a system in the ON state has strong absorption in the visible range and generates *S*-nitrosothiol in the photochemical process. This system can mimic the behaviour of two different kinds of switches, depending on the wavelength used for irradiation (Fig. 5).

In the simplest case light absorption in the visible range (or photogeneration of RSNO) is taken as the output signal. System in the OFF state does not absorb visible light, but switching to the ON state induces strong visible absorption and enables photogeneration of *S*-nitrosothiol. This situation is presented in Fig. 5a. A more complicated switch is obtained, when one takes into account generation of different NO-donors. In this case (Fig. 5b) UV irradiation leads to generation of NO or RSNO, depending on the state of equilibrium (1). When it is shifted to the left (OFF state), photogeneration of nitric oxide due to nitroprusside photochemistry is observed. Any change in the equilibrium leads to $[Fe(CN)_5N(O)SR]^{3-}$ production, whose optical and photochemical properties are different. This system is able to generate NO (in the OFF state) or RSNO (in the ON state) upon UV irradiation, depending on imposed parameters (Fig. 5b). This switch also utilises irreversible photochemical reaction, but the switching process itself is totally reversible. Both kinds of switches can be combined to form more complicated systems, i.e. logical

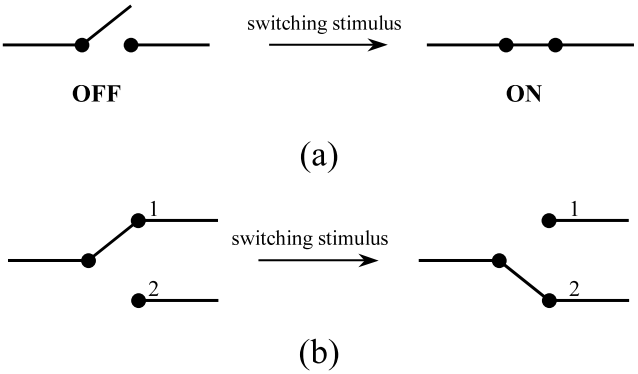
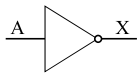
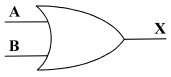
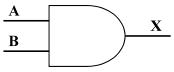


Fig. 5. Molecular switches: (a) simple molecular switch (input: visible light, output: RSNO generation); (b) double switch (input: UV-A light, output 1: NO generation, output 2: RSNO generation), switching stimuli: pH, cations, pressure or temperature.

Table 1
Symbols and truth tables for basic logical gates

Gate	Symbol	Truth table
NOT		A X 0 1 1 0
OR		A B X 0 0 0 1 0 1 0 1 1 1 1 1
AND		A B X 0 0 0 1 0 0 0 1 0 1 1 1

gates—devices able to process several input signals in parallel.

Digital computing circuits usually compute functions of variables, which can have only two values: 0 and 1, also called ON (or TRUE) and OFF (or FALSE), respectively. There are three basic logical gates: NOT, OR and AND. NOT gate computes the negation of the input signal: for input equal to 0 it outputs 1 and vice versa (Table 1). Logical gate OR calculates the logical sum of two or more input signals (Table 1). To set output value to 1, at least one of inputs must be equal to 1. The AND gate computes the logical product of the input values, to set the gate in the ON state all the inputs should be in the ON state, too. Other gates are just combinations of these three basic units, e.g. NAND is a combination of AND and NOT, NOR—of OR and NOT etc.

The first step in mimicking digital units is careful assignment of logical 0 (or FALSE) and 1 (TRUE) levels to specified values of the chemical or physical quantities [1,2,6,58–62]. To obtain the desired switching properties of the system, some parameters must be initially adjusted to a proper level. To switch the studied system from the OFF to the ON state (cf. Fig. 1) at ambient temperature and pressure it is necessary to maintain pH and cation concentration at a high enough level (pH > 9, and $[M^+] \geq 0.1$ M, preferably $M^+ = Cs^+$, Rb^+ or K^+) [36]. The assignment of pH and $[M^+]$ as input parameters leads to the conclusion that the system behaves like an AND logical gate (Fig. 6a) if visible light absorption with λ_{max} at 526 nm is treated as the output signal.

The OR logical gate (Fig. 6b) calculates the logical sum of input parameters, and can be switched on upon application of the TRUE signal to any of the noninverting inputs or FALSE to inverting input. This gate can also be simulated by the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system, but it requires careful adjustment of initial conditions. All the parameters should be set so that change in any of the parameters

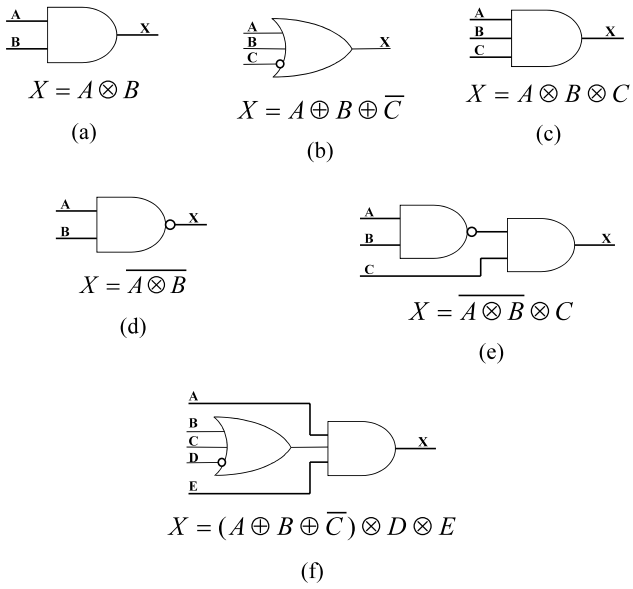


Fig. 6. Digital computing circuits: (a) two-input AND logical gate (A—pH, B—cations, X—light absorption or photoreactivity in visible range); (b) three-input OR logical gate with one inverting input (A—cations, B—pressure, C—temperature, X—light absorption or RSNO generation upon visible irradiation); (c) three-input AND logical gate (A—pH, B—cations, C—visible light, X—RSNO generation); (d) two-input NAND logical gate (A—pH, B—cations, X—NO generation upon UV irradiation); (e) NAND–AND circuit (A—pH, B—cations, C—UV light, X—NO generation); (f) OR–AND computing circuit (A—pH, B—cations, C—pressure, D—temperature, E—visible light, X—RSNO generation).

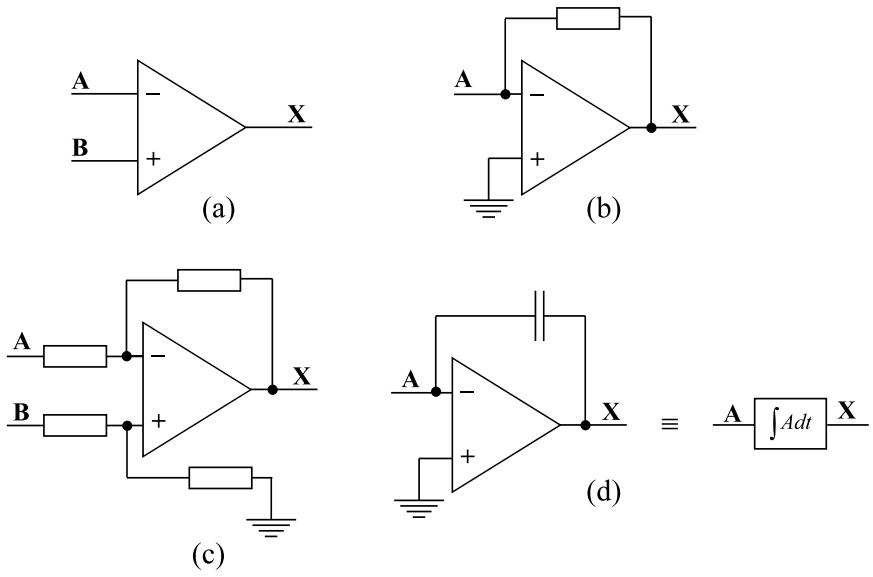


Fig. 7. Analog computing circuits: (a) operational amplifier; (b) follower (A—pressure or cation concentration, X—absorbance at 526 nm); (c) differential amplifier (A—temperature, B—pressure, X—absorbance); (d) integrating circuit with feedback loop and its simplified symbol.

induces switching to the ON state ($X = A \oplus B \oplus C$, where A means pressure, B—cations, C—temperature). As temperature causes an effect opposite to that of pressure and cation concentration, it is assigned to inverting input (cf. differential amplifier, vide infra, Fig. 7c).

Application of light as the input signal leads to several other gates, but they are no longer reversible. Therefore, they cannot be used for any computing purposes, but present an interesting way of controlling the chemical processes: UV-A photolysis of nitroprusside yields NO, but upon addition of thiol and application of any shifting stimuli (vide supra) only RSNO is generated. Photogeneration of RSNO can also be as well achieved upon visible irradiation in the system with equilibrium (1) shifted to the right. If visible light, pH and cations are assigned to input signals the system behaves like a three-input AND gate (Fig. 6c). Photogeneration of NO in the system containing nitroprusside and thiol can be in turn triggered by low pH or low cation concentration. Nitric oxide can be generated at low pH or at low cation concentration, but high pH combined with high cation concentration switches it off. This process is the basis for the NAND gate (Fig. 6d). Here the output signal is assigned to the system ability to photochemical generation of nitric oxide. When light is used as one of input signals, the system behaves like a NAND–AND computing circuit (Fig. 7e).

Due to a high number of different steering parameters it is possible to combine OR and AND logical gates and process up to five different input signals in a simple computing circuit (Fig. 6f). All the systems mentioned above are totally reversible, except the systems in which light is used as one of the input signals.

Not only digital units can be mimicked by the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system. Some analog devices, such as operational amplifiers can be created based on equilibrium (1). The basic unit in analog signal processing is an operational amplifier. It is an electronic device which has two inputs (non-inverting (B) and inverting (A)) and one output (X) (Fig. 7a). The output signal is related to inputs by Eq. 10.

$$X = f(B - A) \tag{10}$$

In the case of an ideal amplifier the output does not depend on absolute values of input signals, but only upon their difference. Depending on configuration, the operational amplifier may have several functions, for example follower, adder and integrator.

The simplest application of an operational amplifier is a follower (Fig. 7b). This is one-input-one-output circuit, the output signal is proportional to the input (11).

$$X = a \cdot A \tag{11}$$

Since the absorbance of the solution containing $[Fe(CN)_5NO]^{2-}$ and $[Fe(CN)_5N(O)SR]^{3-}$ in equilibrium depends linearly on pressure and cation concentration, the system can be used as chemical equivalent of a follower. Selection of pressure or cation concentration as input values and visible absorbance as the output allows mimicking the behaviour of the follower.

A more sophisticated device, whose construction is based on an operational of amplifier is a differential amplifier. This two-input–one-output circuit computes the difference of input signals. Selection of temperature and pressure as input signals and absorption as the output allows construction of a chemical equivalent of a differential amplifier (Fig. 7c). These two stimuli (tem-

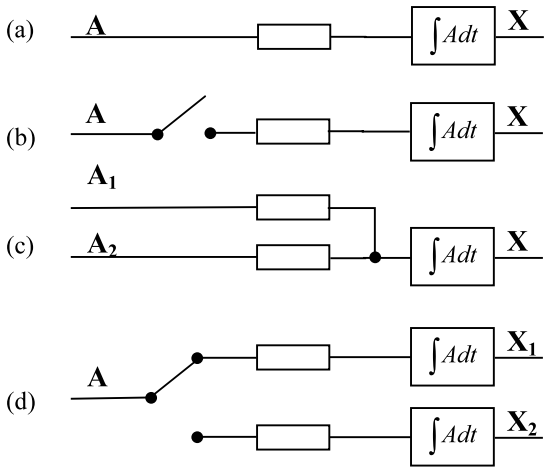


Fig. 8. Integrating circuits: (a) simple (A—visible light, X—NO-donor generation); (b) gated integrating circuit (A—visible light, X—NO-donor generation, gating signal—any switching stimulus except light); (c) dual input integrator (A_1—visible light, A_2—UV light, X—NO-donor generation); (d) dual switchable integrating circuit (A—UV light, switching between A_1 and A_2: any stimulus, except light, X_1—RSNO generation, X_2—NO generation).

perature and pressure) exert opposing effects upon the equilibrium (1), therefore, they can mimic inverting (temperature) and noninverting (pressure) input of the differential amplifier. Simultaneous application of these two input signals changes the absorbance according to equation (12):

$$X = \hat{a}A - \hat{b}B \tag{12}$$

where operators $\hat{a}$ and $\hat{b}$ describe the nonlinear response of the system upon changes in pressure (A) and temperature (B), respectively (cf. Fig. 4).

5. Irreversible systems of phototherapeutic importance

The simulation of some electronic circuits requires irreversible reactions. Irreversible photochemical reactions can be used for example for integration purposes. An integrating circuit is a example of an electronic device, which can easily be mimicked by the system with a irreversible reaction. A real electronic circuit consists of an operational amplifier and a feedback loop with capacitor. The input signal charges the capacitor, and therefore, the output signal is proportional to cumulated electric charge, and hence the time integral of input signal. The $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system imitates an integrating circuit if visible light is taken as the input signal and generation of NO-donors as the output signal (Fig. 7d, Fig. 8a). Photolysis of the system in the ON state leads to photogeneration of RSNO, which is thermally stable and accumulates in solution. Its amount depends on the applied radiation wavelength (λ) and is proportional to the number of photons absorbed and to the quantum yield. At given λ, the system thus integrates input signal (light) versus time (Eq. 13).

$$X = \Phi \int_{t_1}^{t_2} A \, \mathrm{d}t \tag{13}$$

The versatility of the system allows one to build several types of integrating circuits. The simplest one, described above, is presented in Fig. 8a. As mentioned before, the system is photosensitive only to visible light in the ON state (cf. Fig. 1). This property allows one to use the system as a gated integrator (Fig. 8b). Integration of the input signal (visible light) takes place only with the switch in the ON position (i.e. when the equilibrium (1) is shifted towards the $[Fe(CN)_5N(O)SR]^{3-}$ complex). In this case, RSNO generation should be taken as the output signal. To switch on the integrator any of the control stimuli except light (pH, cations, pressure, and temperature) can be used. Moreover, in the ON state the system is sensitive also to UV light, and within the UV-A range can lead to the same products but with a different quantum yield. This feature of the system can be used in a dual input integrating circuit (Fig. 8c), where A_1 refers to visible and A_2 to UV-A light, respectively. In this case the system can compute the integral of the linear combination of two input signals (14).

$$X = \int_{t_1}^{t_2} (\Phi_1 A_1 + \Phi_2 A_2) \mathrm{d}t \tag{14}$$

In the case of UV-A irradiation the system can also mimic a dual switchable integrating circuit (Fig. 8d). Application of UV-A light as the input signal leads to photogeneration of RSNO (system in the ON state, A_2, in Fig. 8d) or nitric oxide (system in the OFF state, A_1 in Fig. 8d) with different quantum yields Φ_1 and Φ_2, respectively. To mimic two parallel switchable integrators it is necessary to monitor simultaneously generation of RSNO (output X_2) and nitric oxide (output X_1) (cf. Eq. 15).

$$\left\{ \begin{array}{ll} X_1 = \Phi_1 \displaystyle\int_{t_1}^{t_2} A \, \mathrm{d}t & \text{(switch in } A_1 \text{ position)} \\ X_2 = \Phi_2 \displaystyle\int_{t_1}^{t_2} A \, \mathrm{d}t & \text{(switch in } A_2 \text{ position)} \end{array} \right\} \tag{15}$$

An electronic equivalent of the system is presented in Fig. 8d.

6. Concluding remarks

The molecular system, presented in this article, in contrast to most hitherto known machines at the molecular level, consists of small, not supramolecular species. Nevertheless, it is able to play the role of a molecular switch and to perform many desired actions simulating a large variety of electronic systems. The system resembles molecular switches based on protonation equilibrium and photoinduced proton transfer in azopyridine and spiropyran, respectively [63].

The systems presented here are just simple examples of different devices useful for computing and signal transformations. The versatility of the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system provides many more possibilities to combine different simple units into more sophisticated systems. Although the rate constant of the reaction (1) is too low [38,47] for fast signal transformation and the system cannot be compared with modern electronic devices, its strong light absorption offers the prospect of application in some optoelectronic units. It is an interesting example of a simple molecular system able to perform complicated calculations. Moreover, it can be regarded as a bridge between biology, chemistry and electronics.

Partial irreversibility of the system plays an important role. Although it may cause some instability of the device working in the photochemical mode, at the same time, it allows generating physiologically important molecules. Moreover, irreversibility is crucial for some analogue applications, such as integration. Combination of a reversible thermal process (1) with irreversible photochemical processes (4–8) may result is such complicated systems as gated or multiple integrating systems. This opens a new aspect in the field of molecular machines and shows that a partially irreversible system may be described in terms of an electronic model.

The most important advantage of the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ molecular system and basis of its further development reside in its potential applicability for biomedical purposes. As generation of nitric oxide and NO-donors is of great and increasing importance for phototherapy, the system can meet expectations, especially because upon irradiation (UV or Vis) it generates NO or various NO-donors (*S*-nitrosothiols, $[Fe(SR)_2(NO)_2]^-$). The physiological activity of these species is different [64–67] and the system guarantees careful control of their production. Thus the physiological activity of the $[Fe(CN)_5NO]^{2-}$–$[Fe(CN)_5N(O)SR]^{3-}$ system can easily be modified and the device can be used as a tunable drug. Due to this potential biomedical application the system should find its place amongst phototherapeutic molecular devices.

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