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Chemically-driven “molecular logic circuit” based on osmium chromophore with resettable multiple readout

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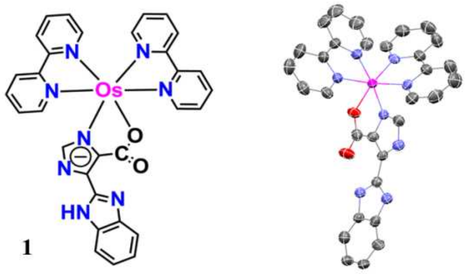
The resettable electro-optical identity of an osmium(II) chromophore has been exploited for integrating miniaturised molecular logic circuits under chemical stimulation. The versatile ‘molecular-probe’ yields multiple outputs using selective stimuli and thus allows precise analysis.

Supramolecular receptors[1] capable of chemical recognition[2] have been realised at nano-scale for meaningful development of molecular gates[3], memory[4] and devices.[5] However, a commercial molecular device seems to be Achilles’ heel without integrated logic circuits.[6] In this context, the innovative approach of logical transformation of discriminating outputs[7] has initiated the leeway for molecular circuit engineering. Importantly, coordination based redox active receptors with multiple outputs are of potential interest for replication of silicon-transistors at molecular level.

Copper, a micronutrient, can afford severe damages such as Wilson's disease, anaemia-symptoms, neutropenia, impaired growth *etc.,* over dose-imbalance.[8] Fluoride prevents dental cavity and osteoporosis but at toxic levels could cause hypocalcaemia and dental or skeletal fluorosis.[9] Importantly, metallic (Cu/Zn) corrosion from fluoridated water during water supply causes the deadly Parkinson and Alzheimer’s diseases.[10] In this viewpoint, chromophores **1** (Scheme 1) was designed with redox $Os(bpy)_2^{2+}$ and conduit imidazole entity for selective multi-dimensional reversible detection of Cu^{2+} and F^-. Interestingly, discrete chemical information was parallely transduced to multiple spectroscopic and visual outputs to integrate logic circuitry.



Scheme 1: Chemical structure and ORTEP representation of **1** (thermal ellipsoids are drawn at 30% probability level). Hydrogen and water molecules are omitted for clarity. Crystal data for 1: $C_{31}H_{22}N_8O_7Os$; M = 808.77; monoclinic; space group P21/c; a = 9.5534(2); b = 25.7853(5); c = 12.6272Å; α = 90; β = 93.47(2); γ = 90°; V = 3104.85(12)$Å^3$; Z = 4; Dc = 1.730 mg m^{-3}; μ = 4.168 mm^{-1}; R_1 = 0.0306; wR_2 = 0.0697, CCDC 995811.

The chromophore **1** was synthesized in reasonable yield (46%), characterized by a full battery of physico-chemical techniques (Fig. S1-S5) and crystallized with P21/c space group and monoclinic point group. The ^{1}H-NMR of **1** in DMSO-d_6 solution exhibits a peak at δ = 14.47 ppm due to the single imidazole proton, indicating at imine group binding motif.

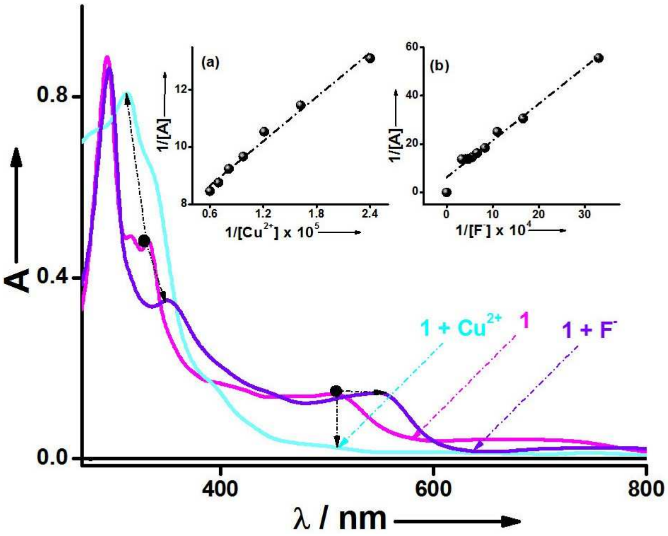


Fig. 1: Representative plot of processing of two different inputs; Cu^{2+} (50 ppb, CH_3CN, **1** + Cu^{2+}) and F^- (30 ppm, CH_3CN, **1** + F^-) *via* **1** (0.98 × 10^{-5}M, CH_3CN, **1**) in UV-vis mode. Inset shows Benesi-Hildebrand plots at λ = 509 and 554 nm with the addition of Cu^{2+} (a) and F^- (b), respectively.

The absorption identity of **1** in acetonitrile exhibits an intense peak at λ = 293 nm (ε = 8.8 × 10^4 M^{-1} cm^{-1}) due to π-π* transition of ligand-centred (LC) band associated with a couple of broad band at λ = 509 (ε = 1.4 × 10^4 M^{-1} cm^{-1}) and 687 nm (ε = 4.1 × 10^2 M^{-1} cm^{-1}) assigned to singlet and triplet metal-to-ligand charge transfer (^{1}MLCT and ^{3}MLCT) tarnsitions, respectively.[11] Interestingly, **1** displays significant modulation *via* UV-vis mode on chemical stimulation with Cu^{2+} and F^- in acetonitrile at ambient temperature. For instance, processing *via* 50 ppb concentration of Cu^{2+} as the input-data produces a bathochromic shift at $\lambda = 293$ nm ($\Delta\lambda = 18$ nm) with emergence of a new shoulder at $\lambda = 337$ nm, associated with remarkable "*turn-off*" modulation at $\lambda = 509$ and 687 nm (5.0 and 4.5- fold) and colourimetric change from light brown to colourless in real time (~15s). This logical output could be attributed to the generation of oxidative osmium (Os^{3+}) species as evident from UV-vis and cyclic voltammetry measurements (Fig. 1).[12] The output was quite input selective as similar inputs *viz.* Zn^{2+}, Pb^{2+}, Ni^{2+}, Na^+, Mn^{2+}, Mg^{2+}, K^+, Fe^{3+}, Co^{2+}, Cd^{2+}, Li^+, Ca^{2+}, Hg^{2+} and Fe^{2+} were inactive (5-10% error, Fig. 2a). The simultaneous processing at multiple wavelengths ($\lambda = 293$, 509 and 687 nm) allows potential option for label-free detection. Importantly, the experiment could be replicated in aqueous medium with similar efficiency (5-8%). On the other hand, applying another input-data comprising of 30 ppm concentration of F^- yields entirely different output signals with MLCT band at $\lambda = 509$ nm as well as shoulder at $\lambda = 325$ nm undergoing bathochromic shift ($\Delta\lambda = 45$ and 25 nm) along with the colourimetric change from light brown to red in real time (~15s) (Fig. 1).

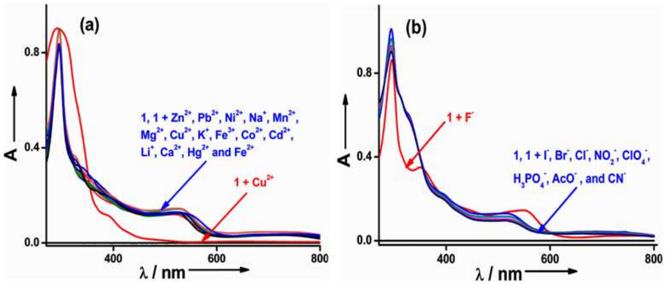


Fig. 2: (a) The UV-vis spectra of **1** (0.98×10^{-5}M, CH_3CN) with Cu^{2+} and other tested metal ions (50 ppb in acetonitrile); (b) The UV-vis spectra of **1** (0.98×10^{-5}M, CH_3CN) with F^- and other tested anions (30 ppm in acetonitrile).

This could be possibly due to interaction of F^- with acidic protons of imidazole unit.[13] No other tested input *viz.* I^-, Br^-, Cl^-, NO_2^-, ClO_4^-, $H_3PO_4^-$, AcO^-, and CN^- could produce the similar output (Fig. 2b). Note that, probe **1** is only suitable for the sensory action in physiological conditions (neutral to slightly acidic medium) as **1** loses selectivity with OH^- ion and hence, can be effectively deployed for biological specimens. Thus, both inputs (Cu^{2+} and F^-) were exclusive and reveal different outputs. Moreover, parallel addition of variety of chemical inputs (in matrix with Cu^{2+} and/or F^-) could not produce any significant change on obtained output (Fig. S6). Importantly, Cu^{2+} was predominating input even in case of parallel processing of both Cu^{2+} and F^- *via* **1**. Moreover, output signals were stationary (Benesi Hildebrand constant: $K_{1+Cu^{2+}} = 2.74 \times 10^5\ M^{-1}$ and $K_{1+F^-} = 4.07 \times 10^4\ M^{-1}$) and show no deviation on increasing the concentration/reaction time up to four times.[14] Notably, the evaluated detection limits ($DL_{Cu^{2+}} = 1.2 \times 10^{-9}$ M and $DL_{F^-} = 2.8 \times 10^{-6}$ M) are superior so far.[15]

Repetitive-action of receptor is highly sought-after for molecular logic functions. The chemical information written on probe **1** by Cu^{2+} and F^- could be erased (>95% reversibility) by H_2O (5µl in 3ml) or H^+ (5µl, 10^{-4}M, 3ml), respectively (Fig. 3). The reversible tuning through **1** was carried out for 3 cycles and showed significant overall regeneration up to ~ 87%. However, even this minor loss of reversibility could be improved by immobilizing this multitasking receptor on the solid support. Interestingly, processing of chemical inputs can integrate various complex logic-circuits operating with different outputs.

As shown in Fig. 4, information processsing with Cu^{2+} (input 1) and H_2O (input 2) as inputs yields an INH (inhibit) logic gate at $\lambda = 509$ nm using a threshold value A = 0.1(absorbance higher/lower than 0.1 will be considered as 0/1, respectively) and IMP (implication) gate at $\lambda = 293$ nm (Fig. S7a, b) using a threshold value A = 0.5 (absorbance higher/lower than 0.5 will be considered as 0/1, respectively). However, on monitoring the information at $\lambda = 554$ and 325 nm on processing of F^- (input 1) and H^+ (input 2) yields coupled INH gates using A = 0.1 (lower "0" and higher "1") and 0.4 (lower "1" and higher "0") as threshold values (Fig. S8a, b).

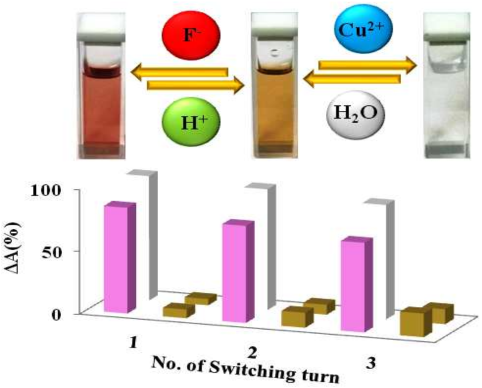
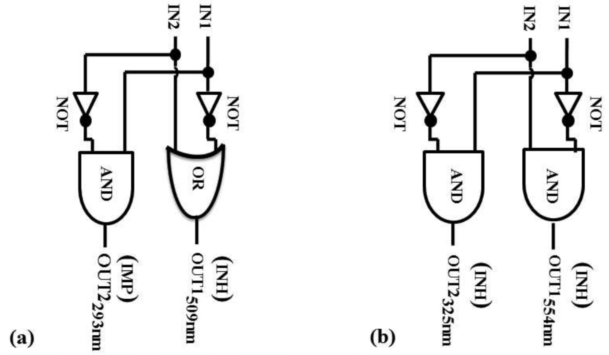


Fig. 3: (a) Pictorial representation of repetitive-processing of Cu^{2+}/H_2O and F^-/H^+ inputs *via* 1 (b) graphical representation of monitoring of ΔA (%) at $\lambda = 509$ and 554 nm as a function of *no.* of switching turns with F^- (pink/light brown pillar) and Cu^{2+} (white/light brown pillar), respectively



In 1 (Cu^{2+})	In 2 (H_2O)	Out 1 (509 nm)	Out 2 (293 nm)
0	0	0	1
0	1	0	1
1	0	1	0
1	1	0	1

In 1 (F^-)	In 2 (H^+)	Out 1 (554 nm)	Out 2 (325 nm)
0	0	0	0
0	1	0	0
1	0	1	1
1	1	0	0

Fig. 4: Logic circuit and truth table for the Boolean inputs (Cu^{2+} and H_2O in acetonitrile, a) and (F^- and H^+ in acetonitrile, b) for **1**.

Multi-output generation by single input could be potentially used for precise and defect-free detection. The recognition propensity of receptor **1** can be monitored *via* optical as well as electrochemical mode. The receptor **1** exhibits dual fluorescence at $\lambda = 371$ and 463 nm on excitation at $\lambda = 293$ nm.[11] Therefore, addition of chemical stimuli to **1** triggers dual modulation in fluorescence identity. The processing of 50 ppb of Cu^{2+} *via* fluorogenic mode demonstrates complete quenching of signal in real time (109-fold at $\lambda = 463$ nm and 8-fold at $\lambda = 371$nm). Differential quenching extent with processing of 30 ppm of F^- in quick time (6-fold at $\lambda = 463$ nm and 371 nm) potentially leads to selective estimation of each stimulus (Fig. 5). The processing of Cu^{2+} was predominant in the mixture of analytes with equal concentration and the written information could be erased (>92% reversibility) by H_2O (Cu^{2+}) or H^+ (F^-) as discussed in case of UV-vis mode. The binding constant (Benesi Hildebrand constant: $K_{1 + Cu^{2+}} = 2.32 \times 10^5$ M^{-1} and $K_{1 + F^-} = 3.56 \times 10^4$ M^{-1}) and detection limit ($DL_{Cu^{2+}} = 1.2 \times 10^{-9}$ M and $DL_{F^-} = 2.8 \times 10^{-6}$ M) evaluated were in agreement with the values obtained by UV-vis data.

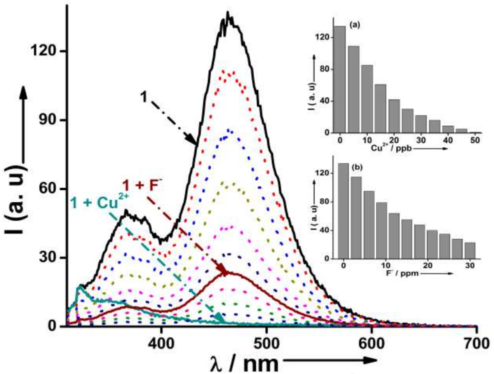
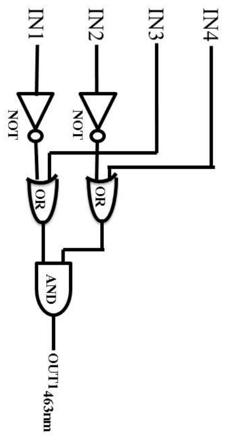


Fig. 5: Fluorogenic processing *via* **1** (0.98×10^{-5} M, CH_3CN) of chemical inputs of 50 ppb Cu^{2+} and 30 ppm of F^- in acetonitrile in real time. Inset shows monitoring of emission intensity at $\lambda = 463$ nm with the addition of Cu^{2+} (a) and F^- (b), respectively.

Assuming Cu^{2+} (In 1), F^- (In 2), H_2O (In 3), and H^+ (In 4), as four inputs, and monitoring the output at $\lambda = 463$ nm (Threshold value = 50 (a.u), intensity higher/lower than 50 (a.u) will be considered as 1/0, respectively) provide a competent molecular system for exclusive processing of four distinct chemical information (Fig. S9). Importantly, chromophore **1** yields distinct response for exclusive and combinatorial information input following the Boolean logic circuit[16] (Fig. 6). The 4-input example based on fluorescence modulation is likely the first example of this type of integrated logic circuit mimic.



In 1 (Cu^{2+})	In 2 (F^-)	In 3 (H_2O)	In 4 (H^+)	OUT (463 nm)
0	0	0	0	1
0	0	0	1	1
0	0	1	0	1
0	0	1	1	1
0	1	0	0	0
0	1	0	1	1
0	1	1	0	0
0	1	1	1	1
1	0	0	0	0
1	0	0	1	0
1	0	1	0	1
1	0	1	1	1
1	1	0	0	0
1	1	0	1	0
1	1	1	0	0
1	1	1	1	1

Fig. 6: Molecular logic circuit constructed using four (Cu^{2+}, F^-, H_2O and H^+) inputs and an exclusive output. Given alongside is the corresponding truth table.

As similar to optical mode, the sensing mechanism of **1** could be monitored in electrochemical mode also with significant reversibility. The receptor **1** shows one electron transfer reversible redox wave at half wave potential ($E_{1/2}$) of 0.35 V with peak to peak separation (ΔE) of 75 mV at 300 mVs^{-1} *vs.* Ag/AgCl.[11] Importantly, addition of chemical inputs exhibits two-way tuning *i.e.,* anodic shift *via* Cu^{2+} ($\Delta E_{1/2} = + 0.14$ V) and cathodic shift *via* F^- ($\Delta E_{1/2} = - 0.15$ V) supporting the proposed sensory action of **1** (Fig. 7). This discriminating behaviour is exclusive and finds eminent applications in low voltage electrochromic devices.

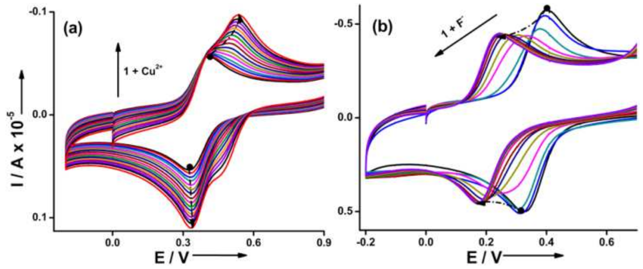


Fig. 7: Cyclic voltammogram of **1** (0.97×10^{-3}M, 0.1 mM TBAP, acetonitrile) on processing of 50 ppb of Cu^{2+} (a) and 30 ppb of F^- in real time.

Conclusions

In summary, stable duo-optical (*chromogenic and fluorogenic*) and electrochemical responses of chromophores **1** were exploited for dual-recognition of cation (Cu^{2+}, 0-50 ppb) and anion (F^-, 0-30 ppm). Moreover, owing to its reversible and rapid output/processing under chemical stimulation, array of logic circuits *viz.* two-input/two- output and four-input/one- output were integrated. The monitoring of outputs *via* multiple modes (*optical, electrochemical, and visual*) provides accurate quantification, widespread utility, and multi-bit information processing at different wavelengths. Importantly, our processor provides label-free detection among matrix of analytes and allows retaining uniqueness of information with no scope of mixing.

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Notes and references

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†*A dedication to Late Dr.Tarkeshwar Gupta.*

Electronic Supplementary Information (ESI) available: X-ray analysis data for **1** (CCDC 995811), Experimental details, characterization, sensing methodology.

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