A chemical circular communication network at the nanoscale†

Beatriz de Luis, Ángela Morellá-Aucejo, Antoni Llopis-Lorente, Feli Sancenón, Tania M. Godoy-Reyes, Reynaldo Villalonga, Elena Aznar, Félix Sancenón and Ramón Martínez-Máñez *abcd

In nature, coordinated communication between different entities enables a group to accomplish sophisticated functionalities that go beyond those carried out by individual agents. The possibility of programming and developing coordinated communication networks at the nanoscale—based on the exchange of chemical messengers—may open new approaches in biomedical and communication areas.

Here, a stimulus-responsive circular model of communication between three nanodevices based on enzyme-functionalized Janus Au–mesoporous silica capped nanoparticles is presented. The output in the community of nanoparticles is only observed after a hierarchically programmed flow of chemical information between the members.

Introduction

Chemical communication is based on the exchange of molecular messengers between different entities. In nature, living cells and organisms rely on chemical communication processes for sustaining vital biological functions. For instance, organelles exchange messengers that allow cellular metabolism; neurons communicate by exchanging neurotransmitters; and physiological functions are regulated by hormone molecules segregated by distant cells. At a larger scale, insects, bacteria and pluricellular organisms communicate with peers by means of pheromones. Communication networks enable a group to share information and act together towards the achievement of a common goal. Considering this aim, coordinated communication displays an essential role as it is necessary to organize the collective behaviour in a defined order to assure efficiency and productivity. In fact, nature life is based on communication processes developed in coordinated communities at the molecular scale involving the use of chemical messengers. As examples of coordinated groups, termite populations and fish shoals have chemically coordinated alarm systems in which a member detects an environment disturbance and secretes alarm molecules. Other members sense this message and expel chemical secretions, subsequently spreading alarm through the community and resulting in the articulation of a collective response (e.g., release of toxic/repellent chemicals or colony recruitment).

Transferring communication capabilities to human-made nanoscale systems has attracted significant attention in recent years due to potential applications in areas such as biomedicine or ICT (Information and Communication Technologies). Compared to traditional telecommunication technologies, chemical communication offers interesting features such as the reduced size of molecular transceivers and receivers, minimal power consumption and the ability to operate in biological and physiological environments. Several micro- and nanocarriers capable of interacting with living systems by means of sending or receiving chemical messengers have been developed. Linear communication between particles or feedback between two particles has also been reported. However, the field is still in its infancy and more complex communication communities should be demonstrated with the future aim to integrate coordinated multicomponent communities of nanodevices with advanced capabilities. Strategies of cooperation and coordination between different nanoparticles may enable sophisticated functionalities that go beyond those carried out by individual agents. However, regardless of the aforementioned advancements made in the last years, the definition of technologies to support practical and useful applications of communication at nanoscale, while essential to motivate further growth of this field in the research community, is still very limited and still scarcely explored.
In this scenario, we report herein a circular model of a multicomponent communication network of nanoparticles based on the exchange of chemical messages. Today it is well recognized the ubiquity of cyclic organization in biology as it provides invaluable resources for controlling and orchestrating biological operations, giving rise to complex temporal dynamics in nature.

For instance, dynamical feedback is observed in biological reaction networks where metabolic processes regulate their activity or resupply the initial substrate in a cyclic manner. Our communication system consists of three enzyme-functionalized Janus Au–mesoporous silica nanoparticles (Au–MSNPs) which display a double receiver-sender behaviour, as depicted in Fig. 1A. The mesoporous face of nanodevice \( S_1 \) (\( S_{1\beta gal} \)) is loaded with the fluorescent dye \([\text{Ru}(bpy)_3]\)Cl\(_2\) and capped with disulfide-containing oligo(ethylene glycol) chains (PEG) acting as gatekeepers, whereas the enzyme \( \beta \)-galactosidase (\( \beta \)gal) is attached to the gold face. In nanoparticle \( S_2 \) (\( S_{2\text{galox}} \)), the enzyme galactose oxidase (galox) is immobilized on the Au face, while the mesoporous silica is loaded with methyl 4-\((\text{bromomethyl})\)benzoate and the mesopores capped with a \( \text{H}_2\text{O}_2 \)-sensitive self-immolative arylboronate derivative (1) which forms a host–guest complex with \( \beta \)-cyclodextrin (Fig. 1B).

As illustrated in Fig. 1A, this circular communication is triggered in the presence of lactose (input). Lactose is transformed into galactose by the enzyme \( \beta \)-galactosidase attached to the gold face of \( S_{1\beta gal} \). Galactose acts as a chemical messenger that is transmitted and sensed by galactose oxidase enzyme on \( S_{2\text{galox}} \) resulting in the formation of galacto-hexodialdose and \( \text{H}_2\text{O}_2 \). Hydrogen peroxide triggers the self-immolative cleavage of the gatekeeper on \( S_{2\text{galox}} \) allowing the delivery of a benzoate.

Fig. 1 (A) Representation of the circular model of communication between three enzyme-functionalized Janus Au–mesoporous silica capped nanoparticles based on the programmed exchange of chemical messengers. (B) Representation of the molecular gatekeepers of each nanodevice. From left to right: disulfide-linked PEG chain, self-immolative arylboronate derivative (1): \( \beta \)-cyclodextrin inclusion complex and benzimidazole-\( \beta \)-cyclodextrin inclusion complex.
Results and discussion

Preparation and characterization of the nanodevices

Janus Au–MSNPs were prepared using gold nanoparticles (of ca. 20 nm obtained by reduction of HAuCl4⋅3H2O with sodium citrate) and MSNPs (of ca. 100 nm MCM-41-type nanoparticles obtained by an alkaline hydrolysis reaction), as adapted from a previous study.31 MSNPs were partially imbedded at the interface of a Pickering emulsion, formed by paraffin wax (oily phase) and water–ethanol (aqueous phase). The un-masked MSNPs surface was decorated with reactive thiol groups, with reaction with (3-mercaptopropyl)trimethoxysilane, on which citrate-capped Au nanoparticles were subsequently attached. After removing the paraffin with chloroform, the starting Janus Au–MSNPs (S0) were obtained. S1 was prepared loading S0 with the [Ru(bpy)3]2+/Ru(bpy)33+ dye and protecting the Au face with 3-mercaptopropionic acid. The resulting solid was reacted with (3-mercaptopropyl)trimethoxysilane, with 2,2’-dipyridyl disulfide and then with O-[2-mercaptoethyl]-O’-methyl-hexyl(ethylene glycol) to give the final capped Janus nanoparticles S1. S1 was obtained from S1 by anchoring β-galactosidase on the carboxylate-modified Au face by means of well-known cross-linking EDC/NHS chemistry resulting in the coupling between the free amino groups of lyase residues from the enzyme and the activated Au carboxyl groups.38 S2 was prepared loading S0 with methyl 4-(bromomethyl)benzoate and adding 3-mercaptopropionic acid to functionalize the gold face. The mesoporous face was reacted with the self-immolative molecule (1) (Fig. 1B) and the system was capped by the formation of an inclusion complex between (1) and β-cyclodextrin (formation constant = 31.1 ± 0.7 M⁻¹).35 For the preparation of S2galox, galactose oxidase was anchored on the Au face of S2 following a similar procedure as previously described for S1gal. S3 was prepared by reacting the mesoporous face of S0 with [3-iodopropyl]trimethoxysilane and then with benzimidazole. The resulting solid was treated with 3-mercaptopropionic acid, loaded with tris[2-carboxyethyl]phosphine and capped with β-cyclodextrin as it threads onto benzimidazole forming an inclusion complex (formation constant = 104 ± 8 M⁻¹).39 S3est was obtained anchoring the esterase enzyme on the Au face of S3 following the above described EDC/NHS chemistry methodology. As control solids, S2blank and S3blank were prepared following the same procedure described for S2galox and S3est respectively but in this case the mesoporous container was not loaded.

The nanoparticles were characterized using standard techniques (Fig. 2, for more details see ESI†). Powder X-ray diffraction patterns at low (1.5 < 2θ < 7) and at high angles (35 < 2θ < 80) of different prepared nanoparticles showed in all cases low-angle reflections of mesoporous silica and high-angle cubic gold characteristic diffraction peaks (see also Fig. S3†). UV/vis of the synthesized Au nanoparticles showed a single surface plasmon absorption band at 524 nm, characteristic of spherically shaped nanospheres with approximately 20 nm diameter that was redshifted to 533 nm in S0 (Fig. S4†). The presence of the mesoporous structure as well as Au nanoparticles was confirmed by transmission electron microscopy (TEM) (Fig. 2B, additional images in Fig. S2†), obtaining similar Au–MSNPs ratios as previously reported.38 N2 adsorption–desorption isotherms of the calcined MSNPs and Janus Au–MS nanoparticles S0 showed an adsorption step at intermediate P/P0 value 0.3 (Fig. S5†), which is characteristic for mesoporous solids with empty pores. Application of the BET model resulted in a value for the total specific surface of 1079 m² g⁻¹ for calcined MSNPs and 802 m² g⁻¹ for S0. Pore sizes and total pore volumes were calculated with the BJH model (Table S1†). The hydrodynamic size and zeta potential of different solids were measured by dynamic light scattering (DLS) (Fig. 2C and Table S2†). S0 showed a hydrodynamic diameter of 115 ± 4 nm that increased to 133 ± 18 nm, 143 ± 15 nm and 148 ± 18 nm for S1gal, S2galox and S3est respectively, whereas Z potential of S0 was −28.4 ± 0.5 and −31.3 ± 0.9, −26.3 ± 0.4 and −30.4 ± 0.7 for S1gal, S2galox and S3est. From elemental analysis and delivery studies the amounts of different components on the nanoparticles were calculated (Table S3†). The presence of β-galactosidase, galactose oxidase and esterase enzymes on S1gal, S2galox and S3est was confirmed by enzyme activity assays (Fig. S6–S8, see ESI† for details) revealing activities of 0.001 U, 0.124 U and 0.165 U per mg of solid, respectively. TEM-EDX mapping of the final nanodevices S1gal, S2galox and S3est confirmed the presence of the expected atoms in the solids. Images showed that gold surfaces were rich in sulfur atoms, strongly suggesting the preferential localization of the enzymes in the Au face (Fig. 2D, S9–S11†) as they were immobilized by means of 3-mercaptopropionic acid. Moreover, the remarkable presence of sulfur atoms in the whole scaffold S1gal is attributed to the disulfide bonds of the gatekeeper PEG in the mesoporous face. In turn, the slight signal of sulfur atoms in S2galox and S3est is attributed to the [3-mercaptoethyl]trimethoxysilane employed to attach the gold nanoparticles to the silica container during the scaffold synthesis. Boron atoms and nitrogen atoms in S2galox are ascribed to the boronic esters and carbanate groups of the gatekeepers in S2galox, whereas the abundance of nitrogen atoms in S3est is due to the presence of benzimidazole moieties.

Release studies

Individual studies. In a first step, we tested the ability of S1gal, S2galox and S3est nanodevices to recognize the
corresponding input and subsequently deliver their payload. For this, we prepared [Ru(bpy)$_3$]Cl$_2$ (dye) loaded nanoparticles (S$_1$$_{gal}$-$S_2$$_{galox}$-$dye$ and S$_3$$_{est}$-$dye$) and monitored dye release in shaken aqueous solutions at pH 7.5 (20 mM sodium sulfate) in the absence and in the presence of the corresponding input (TCEP for S$_1$$_{gal}$-$S_2$$_{galox}$-$dye$ and methyl 4-(bromomethyl)benzoate for S$_3$$_{est}$-$dye$). Aliquots were taken at scheduled times, centrifuged to remove nanoparticles, and the fluorescent emission band of [Ru(bpy)$_3$]Cl$_2$ was measured at 595 nm ($\lambda_{exc} = 453$ nm). Individual delivery studies revealed payload release in the presence of the corresponding stimulus while imperceptible or very low dye delivery was observed in its absence (Fig. 3). Moreover, several release control experiments were carried out for each nanodevice employing their own chemical trigger as input (positive controls) and the chemical trigger of the other nanocarriers (negative controls) revealing no potential interferences between them (Fig. S12-S14 in ESI†). It was also proved that the presence of the corresponding enzyme in S$_2$$_{galox}$-$dye$ and S$_3$$_{est}$-$dye$ was necessary to achieve the nanodevice gate opening and the subsequent cargo release (Fig. S13 and S14 in ESI†).

**Linear communication between pairs of nanoparticles.**

Afterwards, in a further step to evaluate the feasibility of the communication network, we tested the linear communication between each pair of nanodevices [1–2 (S$_1$$_{gal}$/$S_2$$_{galox}$-$dye$), 2–3 ($S_2$$_{galox}$/$S_3$$_{est}$-$dye$), 3–1 (S$_3$$_{est}$/$S_1$$_{gal}$)]. For doing so, each pair was placed in solution and shaken in the absence and in the presence of the communication activating molecule (i.e. lactose for 1–2, galactose for 2–3, and methyl 4-(bromomethyl)benzoate for 3–1). The corresponding nanoparticle concentration conditions were adjusted considering the activity of immobilized enzymes and the solubility of methyl 4-(bromomethyl)benzoate. As shown in Fig. 4, in the three cases a remarkable output (dye delivery) was observed in the presence of the corresponding chemical trigger while a low signal (dye delivery below 20%) was found in its absence. Besides, we confirmed the inability of lactose input to disrupt the disulfide bonds of the molecular gate on nanoparticle 1 (S$_1$$_{gal}$-$S_2$$_{galox}$-$dye$) (Fig. S12†) demonstrating that...
communication between pair 1–2 relied exclusively on the generation of messenger 1 (galactose) by β-galactosidase. All these experiments verified the establishment of linear communication pathways and successful exchange of chemical messages between pairs of nanodevices.

Circular communication. Finally, we tested the realization of the whole circular pattern of communication (Fig. 1A). For these experiments, the three nanodevices (S1gal, S2galox and S3est) were brought together in aqueous solution (20 mM sodium sulfate, pH 7.5) in the same reaction vessel and divided into two fractions. After one hour of incubation, either water (for blank) or lactose 50 mM were added. Aliquots were taken at scheduled times, centrifuged to remove nanoparticles, and the emission at 595 nm of [Ru(bpy)_3]Cl_2 was measured. As depicted in Fig. 5, there was a continuous steady delivery of the cargo from S1gal in the presence of lactose. In contrast, delivery of less than 20% of the maximum delivery observed was found for the community of nanoparticles in the absence of the communication triggering molecule. From 10 hours ahead, the blank fraction (no input) stabilized whereas in the lactose fraction delivery...
continued sharply increasing until reaching saturation around 16 h. In our design, triggers that open the gating mechanism are orthogonal as the chemical messenger generated in the Au face only opens the gated mesoporous silica nanoparticle to which the Au unit is attached. In such a community of nanoparticles, release of the dye from $S_{1_{\text{bgal}}}$ after the addition of a stimulus (i.e. lactose) only becomes effective after the circular communication of the nanoparticles in the sequence $S_{1_{\text{bgal}}}-S_{2_{\text{galox}}}-S_{3_{\text{est}}}-S_{1_{\text{bgal}}}$.

When building cooperative networks of nanoparticles, it is crucial to understand each component's function and rule out potential side interactions and/or incompatibilities between the communities of nanodevices, resulting for instance in “unintended cross-talk” between nanodevices. In order to discard such effects, we performed additional delivery studies in the same conditions previously described using different combinations with “uncomplete” nanoparticles (i.e., lacking either immobilized enzyme or cargo). As shown in Fig. 6, all combinations tested — $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{est}}}$ (lacking the enzyme on nanoparticle 1, bar B), $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{est}}}$ (lacking the enzyme on nanoparticle 2, bar C), $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3}$ (lacking the enzyme on nanoparticle 3, bar D), $S_{1_{\text{fgal}}}/S_{2_{\text{blank}}}/S_{3_{\text{ext}}}$ (lacking the cargo in nanoparticle 2, bar E), and $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{blank}}}$ (lacking the cargo in nanoparticle 3, bar F) — showed much lower delivery in the presence of lactose compared to the complete community of nanoparticles ($S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{ext}}}$, bar H). When one nanoparticle was not complete, the communication channel was disrupted and information was lost. In addition, we also studied the effect of having the enzymes in the solution instead of anchored to the nanoparticles. In a typical experiment the concentrations of the nanoparticles in the sequence $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{est}}}$ were added to the mixture. As observed in Fig. 6 (bar G), the output signal (i.e. $[\text{Ru(bpy)}_3]^2\text{Cl}_2$ release) of the combination $S_{1}/S_{2}/S_{3}/S_{3}/S_{3}$ free enzymes was significantly lower compared to the response of the complete community which is ascribed to the dilution of the (free) enzyme-generated species in the solution. Moreover, the combinations $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{ext}}}$ (lacking a galactose oxidase on nanoparticle 1 and $S_{1_{\text{fgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{free}}}$ esterase on nanoparticle 3) (Table S4 in ESI†) system in the absence (bar A) and the presence (bar K) of lactose (50 mM) is also displayed for comparative purposes. Communication was successfully achieved only when all components were present (bar K). Error bars correspond to the s.d. from three independent experiments.

The behaviour of this circular model of communication between three nanodevices can be expressed in a Boolean logic table of 6 elements:29,40 (i.e. the triggering species (lactose), enzyme $\beta$-galactosidase, enzyme galactose oxidase, cargo of nanoparticle 2 (methyl 4-(bromomethyl)benzoate), enzyme esterase and cargo of nanoparticle 3 (TCEP)). Among the 64 possible entries, only the combination of fully-equipped nanodevices $S_{1_{\text{bgal}}}/S_{2_{\text{galox}}}/S_{3_{\text{ext}}}$ leads to a circular communication and efficient $[\text{Ru(bpy)}_3]^2\text{Cl}_2$ release (Tables S4 and S5 in ESI†).

**Efficiency studies.** Communication efficiency, process efficiency and information loss are relevant aspects that should be
considered when designing logic (chemical) communication systems. Three main processes/logical connections can be defined in our circular communication system: (i) connection 1–2 ($S_{1gal}$-$S_{2galox}$), (ii) connection 2–3 ($S_{2galox}$-$S_{3est}$) and (iii) connection 3–1 ($S_{3est}$-$S_{1gal}$). Thus, the circular communication involves information transmission from one site to another in a hierarchical way following the order 1–2–3–1. In such a circuit, maximum communication efficiency would produce the maximum dye release from site 1. Accordingly, we evaluated the efficiency of the circular information transmission by comparing the output of the 1–2–3–1 process to the maximum possible output from site 1, and also determined the communication efficiency of sections of the circuit, *i.e.* pathway 2–3–1 and pathway 3–1 by external activation on site 2 and site 3, respectively (see Fig. 7A). For doing so, we ran delivery studies in parallel; (i) the dye-loaded nanoparticle $S_{1gal}$ with TCEP as input set the maximum output (cargo delivery) as 100% efficiency; (ii) measuring cargo delivery from $S_{1gal}$ in the $S_{3est}$-$S_{1gal}$ pair with methyl 4-(bromomethyl)benzoate as input allowed to calculate the 3–1 efficiency, (ii) whereas measuring cargo delivery from $S_{1gal}$ in the $S_{2galox}$-$S_{3est}$-$S_{1gal}$ system with galactose or lactose as inputs allowed calculation of the communication efficiency of the 2–3–1 and 1–2–3–1 processes, respectively. Cargo delivery from $S_{1gal}$ without input was set as the background release. From these communication efficiency data the efficiency for each 1–2, 2–3 and 3–1 communication step (process efficiency) was also calculated (Fig. 7B) (see ESI† for further information). For clarification, the different processes have been schematically represented in Fig. 7C. All the experiments were carried out with the same methodology, nanoparticle concentrations and input concentration (50 mM) than that followed in the experiment of Fig. 5 (details in ESI†). The results show that, as expected, the communication efficiency decreases by adding members (communications sites) and processes (connections) to the communication pathway resulting in certain chemical information loss (Fig. 7A and S15†). For instance, as depicted in Fig. 7A, dye delivery from 1 (i.e. $S_{1gal}$) in 3–1 reached maximum efficiency at 12 h whereas information transmission and delivery from 1 in the 2–3–1 section and the 1–2–3–1 circuit remain lower. In addition, at all times, communication efficiencies follow the tendency 3–1 > 2–3–1 > 1–2–3–1. In terms of information degradation after 24 h, no loss is observed for the shortest pathway (3–1) whereas it increases with the number of communication sites (members of the network), with 10% loss and 33% loss for 2–3–1 and 1–2–3–1 respectively (Fig. S15†). Information degradation within complex networks has been also observed by others both in solution and within immobilized communities.41,42 Moreover, process efficiency (Fig. 7B) shows that process 1–2 quickly reaches values of ca. 60–70% and remains approximately constant with time. It can also be observed that the main rate limiting process in our system is the connection 2–3.

Altogether, the results described in this section illustrate how the analysis of processcommunication efficiencies can help understand the complex behaviour of communication systems, identify critical steps, and facilitate the design of optimized networks. In addition, chemical communication networks could be affected by spatial effects such as the relative distance between nanodevices/communication sites. Molecular messengers could be diluted in the medium before reaching its target,41 directional information flow over distances in molecular communication circuits would require a fine control over the location of interacting nanodevices and messenger diffusion kinetics should be considered. In this study, we have conducted the experiments under stirring of solutions containing nanodevices; thus, diminishing the effect of particle location. Notwithstanding,
other works about chemical communication within communities of immobilized abiotic elements using microfluidic technologies have observed the importance of controlling geometrical patterning, chemical input concentrations and flow rate. Although so-far scarce, further studies in this direction will be important for advancing towards the design of chemical communication networks of nanodevices with spatiotemporal control over the information transmission.\textsuperscript{52,53}

**Conclusions**

In summary, we present herein a circular model of communication between nanodevices based on enzyme-functionalized Janus Au–mesoporous silica capped nanoparticles. In the community of nanoparticles, the release of a cargo from a first nanoparticle (output) after the addition of a stimulus (i.e. lactose) is only observed after the circular communication of the nanoparticles in the sequence S\textsubscript{1}galS\textsubscript{2}galoxS\textsubscript{3}galS\textsubscript{1}gal as a result of the exchange of chemical messengers between the components of the group. The relatively slow communication (maximum delivery after 16 h) is ascribed to the number of chemical processes that have to occur to communicate, including enzymatic activation of different molecules, cargo diffusion from the pores to the solution and chemical messenger diffusion from one nanoparticle to another. Moreover a calculation of the communication efficiency, process efficiency and information loss for the different steps of the communication path allowed us to better understand the communication network and determine the rate limiting processes. Several are the options to enhance communication; one of them is the use of nanoparticles equipped with nanomotors and several studies in this direction are being carried by us currently.\textsuperscript{44,45} Overall, our network involves three enzymatic processes and the exchange of three chemical messengers (galactose, an ester derivative and the reducing agent TCEP). Only the complete community of nanoparticles is capable of producing the desired output phenomenon (dye release), while incomplete communities do not succeed in transmitting the information. In spite of being similar to a cascade-like system, its potential scope is beyond a typical metabolic pathway because it is not only limited to the chained enzyme substrates and products. For instance, the possibility of encapsulating a cargo enables communication between enzymes that otherwise could not naturally interact. Moreover, nanoparticles can be directed, concentrated in certain places, etc., allowing designing more advance communication systems, when compared with cascade-like system using chained enzymes in diluted solutions. Circular communication could be of relevance for designing networks enabling initiation of the communication and output from the same nanodevice after sequentially-programmed steps of information transmission with other nanodevices, thus potentially allowing feedback – this is an aspect that would not be possible with a linear pathway since signal detection and final response would occur on different sites. Although the presented design is a proof of concept which leads to a dye release as final output instead of the usual dynamical feedback observed in biological reaction cycles, it illustrates the potential of using abiotic nanodevices to design multistep signalling pathways. Our results demonstrate how artificial nanodevices can be connected by means of molecular communication, yielding systems that show a collective synergetic behaviour. Although modelling of the present system was beyond of our scope, advances in the modelling of molecular communications could help in the design and understanding of chemical networks at the micro/nanoscale. A search of different modes of communication within groups of nanoparticles (such as the circular mode of communication reported here) is a key step to further develop more realistic nano-communities to perform specific and complex tasks at the nanoscale. Moreover, the possibility of combining different nanoparticles and communicating them with living organisms\textsuperscript{46–49} would allow to develop swarms of nanodevices able to interact with their neighbours and local environment leading to advanced systems with new cooperative functionalities. This would cause a deep impact in the way we understand the interaction between artificial nanodevices and nanodevices with living systems. We believe that the idea of developing multicomponent nanoscale cooperative communities capable of communicating and performing coordinated may open new directions in the near future in areas such as biomedicine and ICT.\textsuperscript{50–55}

**Conflicts of interest**

There are no conflicts to declare.

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