Program on Nanotechnology Research and Innovation System Assessment
Georgia Institute of Technology

Active Nanotechnology: What Can We Expect?

A Perspective for Policy from Bibliographical and Bibliometric Analysis

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March 2009

Acknowledgements: This research was undertaken at the Project on Emerging Nanotechnologies (PEN) and at Georgia Tech with support by the Project on Emerging Nanotechnologies (PEN) and Center for Nanotechnology in Society at Arizona State University (sponsored by the National Science Foundation Award No. 0531194). The findings contained in this paper are those of the author and do not necessarily reflect the views of Project on Emerging Nanotechnologies (PEN) or the National Science Foundation. For additional details, see http://cns.asu.edu (CNS-ASU) and http://www.nanopolicy.gatech.edu (Georgia Tech Program on Nanotechnology Research and Innovation Systems Assessment).The author wishes to thank Dave Rejeski, Andrew Maynard, Mihail Roco, Philip Shapira, Jan Youtie and Alan Porter.

Executive Summary

Over the past few years, policymakers have grappled with the challenge of regulating nanotechnology, whose novelty, complexity and rapid commercialization has highlighted the discrepancies of science and technology oversight. One of the important lessons learned from this experience has been the crucial role of foresight in governing nanotechnology.

Active nanostructures are a popular categorization of an emerging class of nanotechnology. The National Science Foundation first solicited "Active Nanostructures and Nanosystems" grants in 2005. Policy reports often refer to greater and different types of risks to society caused by the recently emerging novel applications of nanotechnology, including active nanostructures. The scope of this paper is an appraisal of the research literature in active nanostructures.

1. Introduction

Active nanostructures are characterized by an evolving functionality, i.e. their structure or state or function changes during their use. This evolving functionality may be reversible or irreversible. NSF's "Active Nanostructures and Nanosystems" Nanoscale Interdisciplinary Research Team *(*NIRT) grant gives the following examples of active nanostructures- nanoelectromechanical systems (NEMS), nanomachines, self-healing materials, nanobiodevices, transistors, amplifiers, targeted drugs and chemicals, actuators, molecular machines, light-driven molecular motors, plasmonics, nanoscale fluidics, laser-emitting devices, adaptive nanostructures, energy storage devices, and sensors.

The examples make one wonder the basis with which such diverse objects have been grouped together. The answer is that active nanotechnology has largely been a concept in the "visions" for nanotechnology. The use of these visions give policymakers and social scientists a handle on the salient features of the science. Examples of such "visions" include Mihail Roco's four generations of nanotechnology and James Tour's classification of nanotechnology as Passive, Active and Hybrid. It is not hard to see why "visions" can be controversial. Even from a purely technical viewpoint, defining and bounding nanotechnology has been fraught with debate. The translation of complex scientific concepts into lay language cannot be done without implicit normative and technical judgments, which may become contentious.

Despite the differences and criticisms of various visions, active nanotechnology remains a salient category of many. Moreover, the recent NSF NIRT grant has moved active nanotechnology from the realm of "vision" to a funded research program that is likely to spawn commercial products in the near future. Many policy analyses have predicted that forthcoming nanotechnology cannot be governed adequately by existing science and technology policies, but few have developed this theses explicitly stating actual research. For example, a publication of the International Risk Governance Council (IRGC), passive and active nanotechnology were described as distinct risk "frames", in which the risks associated with active nanostructures were unique and challenge the current risk assessment paradigms. The report does not discuss in adequate detail the science on the basis of which this analysis was done. These reports are authored in consultation with knowledgeable technical panels, and may well have a substantive basis for making such claims, but the basis is not clear to a non-scientist reading the report. Moreover, even with the same technical information, the analysis can be done very differently and this information is important to judge its scope.

This paper is a synthesis in the research literature in active nanostructures in order to address this concern. I have developed a typology of the research that is intended to be useful to policymakers, but it is prone to the same (perhaps more) caveats than similar analyses done by experts. At the very least, this paper draw attention to some interesting current research in nanotechnology. Basic bibliometric analysis has been done to complement this analysis.

2. Methodology

It was a challenge to bound "active nanotechnology". The NSF "Active Nanostructures and Nanosystems" grant solicitation was used as the main definition, along with explanations of the concept by Dr. Mihail Roco of NSF and Dr. James Tour of Rice University. The National Science Foundation (NSF) 's Fast Lane and National Institutes of Health (NIH)'s CRISP databases were searched for recent grants with the keywords " active nano*".

The Science Citation Index of the Web of Science was used to search current literature. In the beginning, searches were performed using "snowballing": one search suggested the keywords to do another. Preliminary search terms are given in Appendix 1. About 200 relevant review papers from these searches were read to develop an understanding of scientific concepts and discern patterns in the literature. In the light of this background work, the best strategy to obtain active nanostructures appeared to be an AND Boolean operation of two search term categories: Material and Active Principle was carried out. The material search term category includes nano*, fullerene#, quantum dot#, dendri* (referred in the keywords as dendrimer, dendrimers, dendritic architecture and dendritic nanostructure), self assembl* and molecul*[1]. The active principle search term category includes motor, rotor, actuat* (for actuator and actuation), sens* (for sensor and sensing), switch, shuttle, smart, responsive, antenna, wireless, adaptive, memory, plasmon*, device, transistor, valve, "logic gate", transistor, "self healing" and intelligent. Explicit second generation terms like Nanoelectromechanical Systems , NEMS and nanofluidics were also added to the set. The searches were run on SCI EXPANDED

[1] The "molecul*" search word is unique in this methodology from others. It was was included to capture nanotechnology based on polymers, crystals and supramolecules and also key words such as molecular motor, molecular machine, molecular electronics, etc; all of which will play an important role in emerging nanotechnology.

Citation Index of Web of Science from 1995 to 2008. In the nano* searches, the exclusion terms nanospray-ESI, Nanog and nanosecond were used.

The above mentioned search strategy contains active nanostructures, but not exclusively. There are very few keywords exclusively associated with active nanotechnology, and there are some examples cited by experts as “active nanostructures” which are not associated with novel keywords. Each abstract was read in order to determine if it was active nanotechnology, and should be included in the dataset. I claim no expertise in drawing sophisticated distinctions to resolve grey areas – that is the work that challenges scientific experts. An example of one of the grey areas is the distinction between microfluidics and nanofluidics. My judgment stance was **inclusive** - if the microfluidic device had an active nanotechnology component, it was included. This inclusive stance extends to the research papers reviewed; if the bibliographic record (particularly Title, Abstract, Keywords and Keywords Plus) mentioned the material and active principle (or implied it as an application) it was included. Over 21000 records were imported into bibliometric software Vantage Point for further analysis. A description of the software is available in Appendix 2. Bibliometric analysis was done in the CNS-ASU group at Georgia Tech.

I would like to clarify the caveats with this methodology. While we have attempted to compile an exhaustive database of active nanostructures, we can only claim to have a representative dataset. For one, there are numerous permutations of the Material and Active Principle. Moreover, there are very few terms explicitly associated with active nanostructures and other higher generation nanotechnology (e.g. Nanoelectromechanical Systems, Nanofluidics, etc). Even with exclusion terms, there is a high degree of convergence between nanotechnology and other disciplines (which is likely to get exaggerated in the future). In other words, it is not possible to automate the process of building a database of active nanostructures without reading the abstracts. Here my own moderate scientific credentials are open to question. Alternative approaches were considered for a systematic way to get a representative set of active nanostructures, but all of them had shortcomings. The specific claim that I make are that my dataset contains many active nanotechnology examples, and some false positives.

3. Bibliometric analysis

The top 25 journals in publishing active nanotechnology in the dataset are given in Table 1.

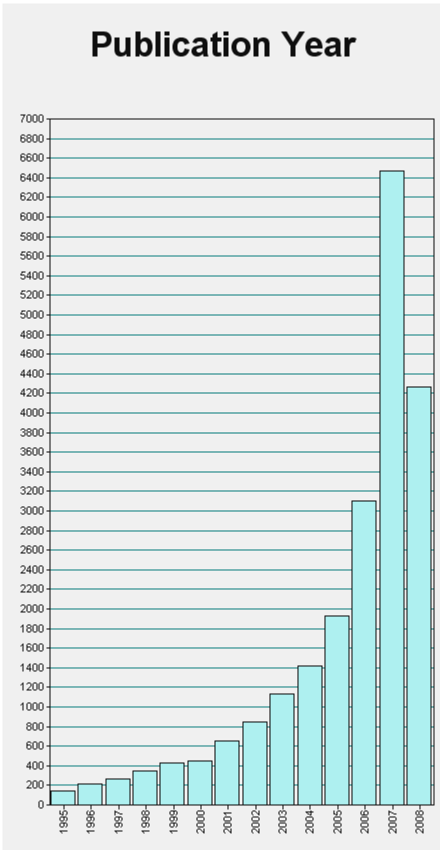
Table 1. Top 25 journals publishing papers on active nanotechnology

Rank	Journals	Number of Records
1	APPLIED PHYSICS LETTERS	1027
2	NANOTECHNOLOGY	582
3	PHYSICAL REVIEW B	515
4	LANGMUIR	505
5	JOURNAL OF APPLIED PHYSICS	478
6	SENSORS AND ACTUATORS B-CHEMICAL	470
7	JOURNAL OF PHYSICAL CHEMISTRY C	447
8	NANO LETTERS	432
9	JOURNAL OF THE AMERICAN CHEMICAL SOCIETY	427
10	ANALYTICAL CHEMISTRY	326
11	BIOSENSORS & BIOELECTRONICS	296
12	THIN SOLID FILMS	272
13	ADVANCED MATERIALS	263
14	MACROMOLECULES	254
15	CHEMISTRY OF MATERIALS	241

16	JOURNAL OF NANOSCIENCE AND NANOTECHNOLOGY	234
17	SYNTHETIC METALS	229
18	JAPANESE JOURNAL OF APPLIED PHYSICS PART 1-REGULAR PAPERS SHORT NOTES & REVIEW PAPERS	221
19	JOURNAL OF PHYSICAL CHEMISTRY B	218
20	JOURNAL OF MATERIALS CHEMISTRY	216
21	ADVANCED FUNCTIONAL MATERIALS	193
22	PHYSICAL REVIEW LETTERS	184
23	PHYSICA E-LOW-DIMENSIONAL SYSTEMS & NANOSTRUCTURES	179
24	MICROELECTRONIC ENGINEERING	177
25	JOURNAL OF VACUUM SCIENCE & TECHNOLOGY B	161

The publication trends in active nanotechnology from 1995 through July 2008 are given in Table 2.

Table 2. Publication trends in active nanotechnology from 1995- July 2008



(Image created using Vantage Point)

The top 25 countries publishing in the area of active nanotechnology are given in Table 3.

Table 3 Top 25 countries in active nanotechnology

Rank	Country	Number of records
1	USA	6926
2	China	2898
3	Japan	2626
4	Germany	1767

5	South Korea	1461
6	UK	1225
7	France	998
8	Italy	661
9	Taiwan	603
10	India	581
11	Canada	561
12	Spain	550
13	Switzerland	472
14	Netherlands	440
15	Russia	413
16	Australia	374
17	Sweden	353
18	Singapore	305
19	Israel	247
20	Belgium	184
21	Poland	174
22	Denmark	171
23	Brazil	163
24	Austria	152
25	Greece	109

The top 25 journal keywords (distinct from author keywords) in the area of active nanotechnology are given in Table 4.

Table 4 Top 25 journal keywords in active nanotechnology

Sno	Journal Keywords	Number of Records
1	FILM	1094
2	DEVICE	880
3	FABRICATION	656
4	SENSOR	648
5	ARRAY	587
6	NANOPARTICLE	580
7	SURFACE	544
8	ADSORPTION	499
9	CARBON NANOTUBE	477
10	BIOSENSOR	454
11	FIELD-EFFECT TRANSISTOR	453
12	TRANSPORT	452
13	GROWTH	447
14	THIN-FILM	419
15	SYSTEM	410
16	TRANSISTOR	407
17	POLYMER	380
18	CONDUCTION	351
19	BEHAVIOR	349
20	SELF-ASSEMBLED MONOLAYER	347

21	ELECTRODE	342
22	SPECTROSCOPY	309
23	PARTICLE	303
24	MOLECULE	298
25	DNA	297
26	POLYMER CONJUGATE	272

It can be observed that many of these keywords are common to nanotechnology in general. Table 5 contains journal keywords associated with the most innovative research.

Table 5 Journal keywords associated with the most innovative research

SENSOR(648)	POLYMER SOLAR-CELLS(8)	SMALL PARTICLES(4)	CHEMICAL OSCILLATOR(2)
DEVICE(880)	SMART POLYMERS(8)	SMART NANOTUBES(4)	CHEMICAL-SENSING MATERIALS(2)
BIOSENSOR(454)	AMPEROMETRIC IMMUNOSENSOR(7)	SUPRAMOLECULAR MACHINE(4)	CHEMOMECHANICAL SYSTEMS(2)
LIGHT-EMITTING DIODE(198)	AMPEROMETRIC TRANSDUCTION(7)	THERMAL ACTUATOR(4)	CHIRAL MEMORY(2)
GAS SENSOR(157)	ARRAY BIOSENSOR(7)	VAPOR-SENSING PROPERTIES(4)	CHIRALITY-MEMORY MOLECULE(2)
CHEMICAL SENSOR(125)	CATALYTIC NANOMOTORS(7)	ACOUSTIC-WAVE DEVICES(3)	CHIROPTICAL MOLECULAR SWITCH(2)
OSCILLATOR(79)	ION-SELECTIVE ELECTRODES(7)	ADAPTIVE SILVER FILMS(3)	COMPOSITE ACTUATORS(2)

PH(69)	MOLECULARLY IMPRINTED POLYMER(7)	AMPEROMETRIC GLUCOSE SENSOR(3)	COMPOSITE BIOSENSOR(2)
ARTIFICIAL MUSCLE(68)	NANOMACHINE(7)	AMPEROMETRIC SENSOR(3)	COMPOSITE VAPOR DETECTORS(2)
MICELLE(67)	ADDRESSABLE POTENTIOMETRIC SENSOR(6)	ANTENNA COMPLEX(3)	DNA BIOSENSORS(2)
MOTOR(67)	AMPHIPHILE NANOFIBERS(6)	APTAMER-BASED SENSORS(3)	DNA PIEZOELECTRIC BIOSENSOR(2)
NANOELECTROMECH ANICAL SYSTEMS(54)	AMPHIPHILIC BISTABLE ROTAXANES(6)	APTASENSOR(3)	DRIVEN MOLECULAR SHUTTLE(2)
PLASMON RESONANCE(53)	BIOSENSOR TECHNOLOGY(6)	ARTIFICIAL NOSE(3)	DRUG-DELIVERY DEVICES(2)
SENSING PROPERTY(52)	CONJUGATED POLYMER ACTUATORS(6)	ARTIFICIAL PHOTORECEPTOR(3)	FIBEROPTIC BIOSENSOR(2)
IMMUNOSENSOR(51)	DOUBLE-CROSSOVER MOLECULES(6)	ARTIFICIAL PHOTOSYNTHETIC ANTENNA(3)	FIBEROPTIC GLUCOSE BIOSENSOR(2)
LOGIC(49)	ELECTROLUMINESCENT POLYMERS(6)	BISTABLE DEVICES(3)	GLUCOSE-OXIDASE BIOSENSOR(2)
MACHINE(47)	ELECTROMECHANICAL ACTUATORS(6)	BROWNIAN RATCHET(3)	GUEST-HOST SYSTEMS(2)
AMPEROMETRIC BIOSENSOR(42)	ELECTROMECHANICAL SYSTEMS(6)	CHEMILUMINESCENT SENSOR(3)	HOST-GUEST CHEMISTRY(2)
LIGHT-EMITTING DEVICE(42)	FREE ELECTROCHEMICAL DETECTION(6)	CHIRAL RECOGNITION(3)	HYBRID BILAYER-MEMBRANES(2)
AMPEROMETRIC DETECTION(39)	MOLECULAR ADAPTER(6)	COLORIMETRIC BIOSENSOR(3)	HYBRID DEVICES(2)

BLOCK-COPOLYMER MICELLES(39)	PIEZOELECTRIC ACTUATOR(6)	COMPLEMENTARY LOGIC GATES(3)	HYBRID MICROGELS(2)
ORGANIC ELECTROLUMINESCENT DEVICE(37)	RESPONSIVE PROPERTIES(6)	ELECTROACTIVE POLYMER(3)	HYDROPHILIC SURFACES(2)
PHOTOINDUCED ELECTRON-TRANSFER(34)	RESPONSIVE SURFACE(6)	ELECTROLYTE ACTUATOR(3)	IMPEDIMETRIC IMMUNOSENSOR(2)
PHOTODIODE(33)	SELECTIVE SOLVENT(6)	FLOW SENSOR(3)	LINEAR MOTOR-MOLECULES(2)
PHOTOELECTROCHEMICAL CELL(32)	SENSING MATERIAL(6)	FUNCTIONAL CAPSULE MEMBRANES(3)	MECHANOCHEMICAL SYNTHESIS(2)
PLASTIC SOLAR-CELLS(32)	SUPERHYDROPHILICITY(6)	FUNCTIONAL MATERIALS(3)	MECHANOCHEMISTRY (2)
GAS-SENSING PROPERTIES(30)	SUPRAMOLECULAR HYDROGEL(6)	FUNCTIONAL POLYMERS(3)	MICROMECHANICAL CANTILEVER(2)
SHUTTLE(30)	THERMORESPONSIVE POLYMER(6)	GLUCOSE-SENSITIVITY(3)	MODULATED OPTICAL NANOPROBES(2)
MOLECULAR MOTOR(29)	THERMOSENSITIVE HYDROGEL(6)	HIGHLY SENSITIVE DETECTION(3)	MOLECULAR DEVICE(2)
ELECTROCATALYSIS(28)	ACTIN-BASED MOTOR(5)	HUMIDITY SENSING PROPERTIES(3)	MOLECULAR INFORMATION-STORAGE(2)
AMORPHOUS MOLECULAR MATERIAL(26)	CHEMILUMINESCENCE DETECTION(5)	HYDROPHOBIC MAGNETIC NANOPARTICLES(3)	MOLECULAR MUSCLES(2)

NANOMECHANICAL RESONATOR(24)	CHEMIRESISTOR SENSOR(5)	LIGHT-EMITTING TRANSISTORS(3)	MOLECULAR RECTIFICATION(2)
SENSITIVE HYDROGELS(24)	COMMAND SURFACE(5)	LIGHT-HARVESTING DENDRIMERS(3)	MOLECULAR RECTIFIER(2)
ELECTROCHEMICAL SENSOR(23)	CONTRACTING MUSCLE(5)	LIGHT-SENSITIVE PHOTOCATALYST(3)	NANOPARTICLE MOLECULAR SENSORS(2)
ELECTRON TRANSISTOR(23)	COPOLYMER BRUSHES(5)	LOCALIZED EMBEDDING PEBBLES(3)	NANOSCALE ELECTROSTATIC ACTUATORS(2)
RESPONSIVE POLYMER(23)	ELECTROCHEMICAL DNA BIOSENSOR(5)	MOLECULAR COMPUTATION(3)	NANOTHERMOMETER (2)
BIOMOLECULAR MOTOR(21)	ELECTROCHEMICAL IMMUNOSENSOR(5)	MOLECULAR FLUORESCENCE(3)	NANOVALVE(2)
MOLECULAR MACHINE(19)	ELECTROGENERATED CHEMI-LUMINESCENCE(5)	MOLECULAR HETEROJUNCTIONS(3)	OPTICAL ANTENNAS(2)
RESPONSIVE CONTROLLED-RELEASE(19)	FUNCTIONALIZED MESOPOROUS SILICA(5)	MOLECULAR MECCANO(3)	OPTICAL BIOSENSOR LITERATURE(2)
NANOSCALE OPTICAL BIOSENSOR(18)	HYDROPHILICITY(5)	MOLECULAR PHOTOVOLTAIC DEVICES(3)	OPTICAL IMMUNOSENSOR(2)
ELECTROWETTING-BASED ACTUATION(17)	HYDROPHOBIC SURFACE(5)	MOLECULAR PHOTOVOLTAICS(3)	OPTICAL SWITCH(2)
FLUORESCENT SENSOR(17)	HYDROPHOBICALLY-MODIFIED POLY(N-ISOPROPYLACRYLAMIDE)(5)	MOLECULAR SPINTRONICS(3)	OPTICAL-FIBER DEVICES(2)

LABEL-FREE DETECTION(17)	HYDROPHOBICALLY-MODIFIED POLYELECTROLYTES(5)	MOLECULE DETECTION(3)	OPTICALLY-ACTIVE POLYANILINE(2)
MOLECULAR SHUTTLE(17)	MACHINE PROTOTYPES(5)	NANOELECTROMECHANICAL OSCILLATORS(3)	PH-DEPENDENT DEGRADATION(2)
BIOMIMETIC SENSORS(16)	MICROCANTILEVER SENSOR(5)	NANOMECHANICAL PROPERTIES(3)	PH-RESPONSIVE BEHAVIOR(2)
ENZYME ELECTRODE(16)	MOLECULAR ELECTRONIC DEVICE(5)	NANOMECHANICAL RESONANT STRUCTURES(3)	PH-RESPONSIVE MICELLES(2)
PHOTOPOLYMERIZATION(16)	MOLECULAR JUNCTIONS(5)	NANOTUBE ACTUATORS(3)	PH-RESPONSIVE MICROGELS(2)
ELECTROPHOSPHORESCENT DEVICES(15)	MOLECULAR LOGIC(5)	NEMS DEVICES(3)	PH-SENSITIVE POLYMER(2)
HYDROGEN SENSOR(15)	MOLECULAR NANOSTRUCTURE(5)	OPTICAL NANOSENSORS(3)	PHOTOACTIVE ROTAXANES(2)
NANOMECHANICS(15)	MOLECULAR RULER(5)	ORGANIC-INORGANIC NANOCOMPOSITES(3)	PHOTOCHEMICAL PROPERTIES(2)
SENSING CHARACTERISTICS(15)	PH-SENSITIVE LIPOSOMES(5)	PEPTIDE NANOTUBES(3)	PHOTOCHEMICAL SWITCHING BEHAVIOR(2)
GLUCOSE BIOSENSOR(14)	PHOTOSYNTHETIC ANTENNA(5)	PH-RESPONSIVE PROPERTIES(3)	PHOTOINDUCED BENDING BEHAVIOR(2)
MOLECULAR ELECTRONICS(14)	PIEZOELECTRIC IMMUNOSENSOR(5)	PH-SENSITIVE SYSTEM(3)	PHOTOMODULATED REFLECTANCE(2)
MOLECULAR MECHANICS(13)	PORPHYRIN ARRAYS(5)	PHOTORESPONSIVE POLYMERS(3)	PHOTOREFRACTIVE MATERIALS(2)

MOLECULAR SWITCH(13)	QUANTUM COMPUTER(5)	PIEZOELECTRIC NANOGENERATORS(3)	PHOTOREFRACTIVE POLYMERS(2)
SPIN-VALVE SENSORS(13)	ROTARY MOTOR(5)	PIEZORESISTIVE SENSORS(3)	PIEZOELECTRIC BIOSENSOR(2)
STIMULI-RESPONSIVE POLYMER(13)	SCHIZOPHRENIC DIBLOCK COPOLYMER(5)	PLASMON RESONANCE BIOSENSOR(3)	PIEZOELECTRIC MICROPUMP(2)
SUPRAMOLECULAR NANOVALVE(13)	SHUTTLE MEMORY DEVICE(5)	PLASMON RESONANCE IMMUNOSENSOR(3)	POLY(ACRYLIC ACID) BRUSHES(2)
TECHNOMIMETIC MOLECULES(12)	SINGLE-ELECTRON MEMORY(5)	POLYMERIC BIOMATERIALS(3)	POLY(ETHYLENE GLYCOL)-CONTAINING HYDROGELS(2)
LIGHT-HARVESTING COMPLEX(11)	SMART DUST(5)	POLYMERIC ELECTRONICS(3)	PROTEIN BIOSENSOR(2)
MOLECULAR MATERIALS(11)	SUPERHYDROPHOBICITY(5)	POTENTIAL ELECTROLUMINESCENT MATERIALS(3)	REDOX SENSORS(2)
MOLECULAR ROTOR(11)	SWITCH-PEPTIDES(5)	QUANTUM CELLULAR-AUTOMATA(3)	RESONANT-TUNNELING DEVICES(2)
PLASMON RESONANCE SENSOR(11)	SWITCHING DEVICE(5)	REDOX POLYMER(3)	RESPONSIVE MICROGELS(2)
SENSING APPLICATION(11)	THERMOSENSITIVE POLYMER(5)	RESONANCE SENSOR(3)	RESPONSIVE POLYMERIC MICELLES(2)
CARBON NANOTUBE ACTUATORS(10)	AMPHIPHILIC POLYMER(4)	RESPONSIVE GELS(3)	SENSITIVE POLYMERS(2)

DOT CELLULAR-AUTOMATA(10)	ARTIFICIAL PHOTOSYNTHETIC MEMBRANE(4)	RESPONSIVE HYDROGEL(3)	SENSITIVE SUPRAMOLECULAR ASSEMBLIES(2)
ELECTRONIC NOSE(10)	BIODEGRADABLE THERMOSENSITIVE POLYMERS(4)	RESPONSIVE MICRODOMAINS(3)	SENSOR RESPONSE(2)
MOLECULARLY DOPED POLYMERS(10)	CHOLESTEROL BIOSENSOR(4)	RESPONSIVE MOLECULAR SWITCHES(3)	SINGLE-ELECTRON DEVICES(2)
OPTICAL BIOSENSOR(10)	COMPOSITE ELECTROCHEMICAL SENSORS(4)	RESPONSIVE PARTICULATE EMULSIFIERS(3)	SMART(2)
POLYELECTROLYTE BRUSHES(10)	ETHANOL SENSING CHARACTERISTICS(4)	RING OSCILLATORS(3)	SMART APTAMERS(2)
SENSOR ARRAY(10)	FIBER-OPTIC SENSOR(4)	SENSOR SYSTEM(3)	SMART SYSTEMS(2)
THERMALLY RESPONSIVE POLYMERS(10)	FLEXIBLE ELECTRONICS(4)	SUBSTRATE-SELECTIVE POLYMERS(3)	SPIN-LABELED POLYMERS(2)
TURNSTILE DEVICE(10)	FLUOROSENSOR(4)	SUPERHYDROPHOBIC SURFACE(3)	SPR-BASED IMMUNOSENSOR(2)
ACOUSTIC-WAVE SENSOR(9)	FUNCTIONAL DENDRIMERS(4)	SWITCHABLE SURFACE(3)	STIMULI-RESPONSIVE VESICLES(2)
ARTIFICIAL ANTENNA SYSTEMS(9)	HYBRID SYSTEMS(4)	SYNTHETIC NANOPORE(3)	SUPRAMOLECULAR ANTENNA COMPLEXES(2)
HYDROGEN-PEROXIDE BIOSENSOR(9)	LIGHT-HARVESTING ANTENNA(4)	TEMPERATURE-SENSITIVE HYDROGEL(3)	SWELLING RESPONSE(2)
MAGNETORESISTIVE SENSORS(9)	MOLECULAR PHOTOCHEMICAL DEVICE(4)	ZWITTERIONIC BLOCK-COPOLYMERS(3)	SWITCHABLE ION-TRANSPORT(2)
	NANOMECHANICAL CANTILEVER ARRAY(4)	ABSORBENCY SENSOR(2)	TEMPERATURE SENSORS(2)

MOLECULAR SWITCHING DEVICE(9)			
MULTIPORPHYRIN ARRAYS(9)	PHOSPHOLIPID POLYMER(4)	AFFINITY SENSOR(2)	TEMPERATURE-SENSITIVE GELS(2)
NANOELECTRONICS(9)	PHOTOCHEMICALLY DRIVEN(4)	ALCOHOL SENSOR(2)	THERMALLY REVERSIBLE HYDROGEL(2)
NANOWIRE NANOSENSORS(9)	PHOTON TURNSTILE DEVICE(4)	AMPEROMETRIC GLUCOSE BIOSENSOR(2)	THERMALLY-RESPONSIVE POLYPEPTIDES(2)
ELECTRONIC DEVICE(8)	PHOTORESPONSIVE CROWN ETHERS(4)	ARTIFICIAL MOLECULE(2)	THERMOREVERSIBLE POLYMERS(2)
HYDROPHILIC BLOCK-COPOLYMER(8)	PIEZORESISTIVE CANTILEVER(4)	ARTIFICIAL TASTE SENSOR(2)	THERMOSENSITIVE PROPERTIES(2)
NANOCOMPOSITE HYDROGELS(8)	RESPONSIVE BLOCK-COPOLYMER(4)	BIMORPH ACTUATOR(2)	THIN-FILM SENSORS(2)
ORGANIC SOLAR-CELLS(8)	RESPONSIVE DIBLOCK COPOLYMERS(4)	BIOADHESIVE POLYMER(2)	TYROSINASE BIOSENSOR(2)
PH SENSOR(8)	SENSITIVE MEMBRANES(4)	BIOMIMETIC MEMBRANES(2)	VAPOR SENSORS(2)
PH-SENSITIVE HYDROGEL(8)	SENSITIVE PHOTOCATALYST(4)	CARBON NANOTUBE SENSORS(2)	ZNO GAS SENSOR(2)

Table 6 lists the top 25 author keywords 9. Author keywords are the words that the article authors use to describe their own work.

Table 6 Top 25 Author keywords

Sno.	Author keywords	Number of records
1	CARBON NANOTUBE	397
2	BIOSENSOR	299
3	NANOPARTICLE	207
4	MICROFLUIDIC	166
5	ATOMIC FORCE MICROSCOPY	160
6	NANOSTRUCTURE	141
7	SENSOR	140
8	NANOTECHNOLOGY	136
9	GAS SENSOR	130
10	SELF ASSEMBLE	124
11	GOLD NANOPARTICLE	116
12	DYE-SENSITIZED SOLAR CELL	110
13	FIELD-EFFECT TRANSISTOR	103
14	ELECTROLUMINESCENT	101
15	QUANTUM DOT	92
16	COULOMB BLOCKADE	88
17	DNA	86
18	BLOCK COPOLYMER	84
19	ACTUATOR	82
20	HYDROGEL	82
21	FLUORESCENCE	81
22	ELECTROCHEMISTRY	78

23	DRUG DELIVERY	76
24	NANOCOMPOSITE	76
25	PHOTOLUMINESCENCE	70

Table 7 lists the author keywords associated with the most innovative research.

Table 7 Author keywords associated with the most innovative research

biosensor(299)	organic-inorganic hybrid(6)	nanotransistor(3)	liquid crystalline elastomer(2)
sensor(140)	quantum device(6)	optical antenna(3)	low band gap polymers(2)
gas sensor(130)	sensor network(6)	optical biosensor(3)	low bandgap polymer(2)
quantum dot (92)	smart surface(6)	OPTICAL MEMORY(3)	low-humidity sensor(2)
block copolymer(84)	supramolecule(6)	optical waveguide(3)	magnetoresistance effect(2)
actuator(82)	thermoresponsive polymer(6)	organic EL(3)	magnetoresistive biochip(2)
hydrogel(82)	azo-polymer(5)	organic memory(3)	magnetoresistive devices(2)

drug delivery(76)	Brownian ratchet(5)	organic photovoltaic device(3)	magnetoresistive sensor(2)
polymer(69)	bulky shuttle memory device(5)	pH- and temperature-sensitive(3)	mass-sensitive sensors(2)
single electron transistor(68)	DNA sensing(5)	photocatalytic activity(3)	mechanochemistry(2)
conducting polymer(67)	electrochemical immunosensor(5)	photorefractive polymer(3)	mechanotransduction(2)
light-emitting diodes (LED)(64)	electrowetting(5)	photoresponse(3)	memory device(2)
MEMS(61)	fibre-optic sensor(5)	piezoelectric immunosensor(3)	microoptoelectromechanical system (MOEMS)(4)
molecular device(42)	fluorescence resonant energy transfer(10)	polyelectrolyte multilayers(3)	MIP(2)
molecular motor(42)	glucose detection(5)	polymer composite(3)	molecular logic(2)

molecular electronic(41)	glucose sensor(5)	polymer electronics(3)	molecular machinery(2)
chemical sensor(36)	host-guest(5)	polymer micelle(3)	molecular magnets(2)
micelle(34)	hybrid material(5)	polymer sensor(3)	molecular motors theory(2)
immunosensor(33)	ion-selective electrode(5)	polymer therapeutics(3)	molecular nanotechnology from the bottom-up(2)
nanoelectronics(33)	light harvesting(5)	polyurethane elastomer films(3)	molecular photonics(2)
NEMS(31)	LPG sensor(5)	Quantum-dot Cellular Automata(6)	molecular programming(2)
molecular recognition(29)	magnetoelastic(5)	quartz crystal microbalance (QCM)(3)	molecular receptor(2)
poly(N-isopropyl acrylamide)(29)	magnetostriction(5)	responsive release(3)	molecular scale electronics(2)

supramolecular chemistry(27)	molecular memory(5)	reverse micelle(3)	molecular sensing/recognition(2)
organic light-emitting diode(26)	molecular rectifier(5)	ring resonator(3)	molecular transducer(2)
biomimetic(25)	nanoelectrode(5)	semiconductor polymer(3)	molecular transistor(2)
stimuli-sensitive polymer(25)	nanoelectromechanical memory(5)	sensing mechanism(3)	molecular transport(2)
cyclodextrin(24)	nanoprobe(5)	sensor application(3)	nanocomposite hydrogel(2)
hybrid(24)	organic light emitting diode (OLED)(42)	single electron tunneling transistors(3)	nanoelectronic device(2)
thin-film transistor(23)	organic/inorganic interfaces(5)	single-molecule detection(3)	nanomechanical resonator(2)
humidity sensor(22)	oTFT(5)	SMART sensor(3)	nanomechanical sensor(2)
pH-sensitive(22)	PEDOT(5)	smart structure(3)	NOR gate(2)

fiber-optic sensor(21)	polymer light emitting diode(5)	soft material(3)	organic field-effect transistors (OFETs)(4)
glucose biosensor(20)	redox polymer(5)	supramolecular assembly(3)	optical detection(2)
memory(20)	smart coatings(5)	surface plasmon resonance sensor(3)	optical device(2)
molecular switch(20)	smart hydrogel(5)	thermal sensitive(3)	optical glucose sensor(2)
smart polymer(20)	thin film device(5)	thin film sensor(3)	optical immunosensor(2)
organic thin film transistor(19)	active transport(4)	adaptive systems(2)	optical MEMS(2)
artificial muscle(18)	all-optical switch(4)	amorphous hole transporting materials(2)	optical ring resonator(2)
thin-film transistor (TFT)(18)	antenna(4)	amperometric response(2)	optically active(2)
Guest Host Interactions (17)	aptasensor(4)	amphiphilic block copolymers(2)	optode(2)

organic semiconductor based on conjugated molecules(17)	bioelectronic device(4)	amphiphilic copolymer(2)	oral drug delivery(2)
molecular machine(16)	biomolecular interaction(4)	amphiphilic dendrimer(2)	organic electroluminescent diode(2)
organic light emitting device(16)	chemomechanical polymers(4)	antenna arrays(2)	organic electronic device(2)
single electron device(16)	CO gas sensor(4)	antenna systems(2)	organic photovoltaic cell(2)
DNA biosensor(15)	DNA biochip(4)	binary switch(2)	organic-inorganic hybrid composites(2)
smart material(15)	DNA computer(4)	bio-MEMS(2)	organic-inorganic polymer hybrids(2)
DNA chip(14)	elastin-like polypeptide(4)	bio-sensing(2)	peptide nanotube(2)
electrochemical biosensor(14)	electroactive polymer actuator(4)	bioactive material(2)	pH sensitive liposomes(2)

microelectromechanical system (MEMS(14)	electrochromic device(4)	BioFET(2)	pH-/temperature-responsive(2)
organic FET(14)	hybrid method(4)	biological applications of polymers(2)	pH-controlled release(2)
bionanotechnology(13)	hybrid solar cells(4)	biomacromolecule(2)	pH-dependent release(2)
DNA sensor(13)	hydrophobic interaction(4)	biomolecular sensor(2)	pH-responsive release(2)
dye sensitized solar cell(13)	Ionic Polymer Metal Composite(4)	biosensor chip(2)	pH-sensitive nanoparticle(2)
optic sensor(13)	Ion Sensitive Field Effect Transistor (4)	cantilever sensor(2)	pH-sensitive PEG-PE conjugates(2)
porphyrin(13)	light-emitting electrochemical cell(4)	capacitive biosensor(2)	pH-sensitive polymer(2)
quantum computer(13)	light-emitting polymer(4)	capacitive detection(2)	photo-responsive(2)

finFET(12)	light-valve(4)	capacitive sensing(2)	photoactivation(2)
high-electron mobility transistor (HEMT)(12)	magnetic switches(4)	carbon nanotube polymer composites(2)	photoactive(2)
molecular imprint(12)	metal-polymer complexes(4)	carbon nanotube sensor(2)	photoanode(2)
nanodevice(12)	molecular computer(4)	catalytic wheel(2)	photocatalytic degradation(2)
organic electroluminescent device(12)	molecularly doped polymers(4)	ChemFET(2)	photochromic molecule(2)
piezoelectric(12)	optic gas sensor(4)	ChemFET sensor(2)	photochromic polymer(2)
surface enhance Raman scattering(12)	optofluidic(4)	chemical actuator(2)	photodegradation(2)
nanoelectromechanical system(11)	pH-responsive nanogel(4)	chemical detection(2)	photoelectrochromic(2)

electroactive polymer(10)	pH-sensitive hydrogel(4)	chemical engines(2)	photosynthetic antenna(2)
electrochemical detect(10)	piezoelectric biosensor(4)	chemical modified electrodes (2)	phototransistor(2)
electrochemiluminescence (10)	piezoelectric material(4)	chemoresistive sensors(2)	piezoelectric sensor(2)
electroluminescent device(10)	piezoresistive cantilever(4)	CNTFET(4)	piezoresistive sensor(2)
molecular electron devices(10)	quantum wire transistor(4)	CO2 gas sensor(2)	piezoresponse(2)
molecularly imprinted polymer(10)	responsive surface(4)	coupled Brownian motors(2)	porphyrin oligomer(2)
stimuli-responsive polymer(10)	single-molecule studies(4)	electro-active paper (2)	pseudopolyrotaxane(2)
switch(10)	single-molecule transistor(4)	electro-active polymer(2)	Quantum Cellular Automata(2)

thermoresponse(10)	small molecules(4)	electro-optic devices(2)	Quartz Crystal Microbalance sensor(2)
biodegradable polymer(9)	smart(4)	electrochemical device(2)	redox-active(2)
nanoelectromechanical system (NEMS)(12)	superhydrophobic surface(4)	electrochemical surface plasmon resonance(2)	redox-active molecule(2)
optoelectronic devices(9)	surface-enhanced Raman scattering (SERS)(19)	electrochemical switch(2)	responsive drug release(2)
pH sensor(9)	thermal actuator(4)	electrochemiluminescent sensor(2)	responsive films(2)
resonant tunneling diode(9)	thermally responsive material(4)	electrogenerated chemiluminescence (ECL)(2)	responsive hydrogels(2)
surface plasmon resonance (SPR)(9)	thermo-responsive(4)	electrogenerated chemiluminescence (ECL) sensor(2)	responsive materials(2)

thermosensitive(9)	thermo-responsive polymer(4)	electronic device structures(2)	room temperature detection(2)
bioelectronic(8)	thermochromic(4)	electronic memory(2)	sensing layer(2)
biomolecular motor(8)	thermosensitive polymer(4)	electrostrictive material(2)	silicon nanowire transistor(2)
biosensing(8)	bio-sensor(3)	ENFET(2)	small organic molecules(2)
conducting materials(8)	bioactive glass(3)	environment-sensitive hydrogels(2)	smart biomaterials(2)
core-shell polymers(8)	biofuel cell(3)	enzymatic biosensor(6)	smart membrane(2)
diblock copolymer(8)	biomembrane(3)	ferroelectric liquid crystal(2)	smart structural material(2)
label-free(8)	biomotor(3)	ferromagnetic nanodot(2)	spin valve sensor(2)
optical switch(8)	carbon nanotube field-effect transistor (3)	FET-type biosensor(2)	stimuli-responsive gel(2)

organic device(8)	conductive polymer composite(3)	FET-type sensor(2)	stimuli-responsive system(2)
organic solar cell(8)	conformational switch(3)	fin field-effect transistor (2)	stimuli-sensitive(2)
organic transistor(8)	conjugated molecule(3)	flagellar rotary motor(2)	stimuli-sensitive hydrogel(2)
polymer-matrix composites(8)	elastin-like polymer(3)	floating gate memory(2)	superelastic(2)
screen-printed electrode(8)	electroactive(3)	functional membrane(2)	superhydrophobic(2)
amorphous molecular material(7)	electrochemical gate(3)	functional polymer(2)	supported lipid bilayer(2)
amperometric immunosensor(7)	electrochemical polymerization(3)	gas sensing mechanism(2)	supramolecular(2)
biopolymer(7)	electrochemical sensing(3)	gel polymer electrolyte(2)	supramolecular complexes(2)
carbon nanotube field effect transistor(7)	electrogenerated chemiluminescence(3)	genosensor(2)	supramolecular organization(2)

ionic polymer-metal composite(7)	electromechanical actuator(3)	glucose sensing(2)	supramolecular polymer(2)
light-emitting polymer device(7)	electronic nanotechnology(3)	glucose sensitive(2)	surface acoustic wave sensor(2)
linear motor(7)	electrostatic microactuators(3)	H2O2 biosensor(2)	surface actuator(2)
molecular photodiode(7)	environmental sensitivity(3)	H2S gas sensor(2)	surface block dendrimer(2)
polymer brush(7)	flexible electronics(3)	hostguest systems(2)	surface plasmon resonance (SPR) sensor(2)
polymer solar cell(7)	FLUOROPOLYMER(3)	humidity sensing(2)	swelling property(2)
protein-based polymers(7)	foldamers(3)	hybrid biomaterials(2)	switchable rotaxane(2)
smart textile(7)	functionalized carbon nanotube(3)	hybrid integration(2)	tactile sensor(2)
carbon nanotube transistor(6)	heteroatom-containing polymers(3)	hybrid metal oxides/MWCNT(2)	taste sensor(2)

DNA electrochemical biosensor(6)	hybrid organic-inorganic materials(3)	hybrid nanostructures(2)	temperature-/pH-sensitive(2)
elastomer(6)	hydrogen gas sensor(3)	hybrid network(2)	temperature-sensitive polymer(2)
electronic nose(6)	hydrophilic polymers(3)	hybrid organic-semiconductor devices(2)	thermal sensors(2)
fluorescent sensor(6)	hydrophobic(3)	hybrid systems(2)	thermally responsive graft copolymer(2)
functional materials(6)	hydrophobic microdomain(3)	imprinted polymer(2)	thermoluminescence(2)
microelectromechanical devices(6)	liquid crystal light valve(3)	intelligent biomaterial(2)	thermomechanical actuator(2)
molecular actuator(6)	liquid crystalline polymers(3)	ionic polymer-metal composite (2)	transition-edge sensor(2)
molecular rotor(6)	MEMS/NEMS(3)	light-driven molecular switch(2)	tunable laser(2)

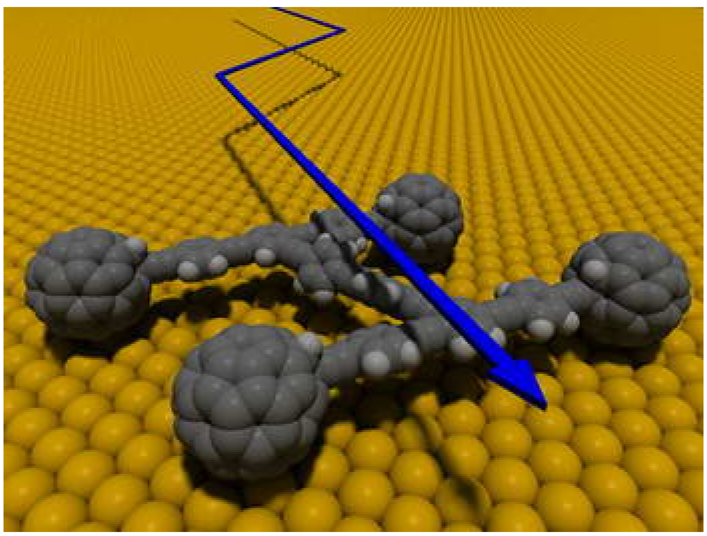
molecular shuttle(6)	metalloporphyrin(3)	light-sensitive(2)	unimolecular electronics(2)
nanobiosensor(6)	modulated release(3)	linear actuator(2)	unimolecular micelle(2)
nanocantilever(6)	molecular conduction(3)	linear piezomotor(2)	unimolecular rectifier(2)
optical tweezers(6)	molecular sensor(3)	liquid actuation(2)	wireless sensor networks(2)

4. Literature Perspectives

Scientific progress in nanotechnology is driven by progress in three streams of scientific endeavor: a) Vertical integration in individual scientific disciplines b) Horizontal integration across scientific disciplines at the nanoscale c) Tools of manipulation at the nanoscale. Nanotechnology based on motor proteins [2]can be used to illustrate this conceptualization. Advances in the biological sciences, particularly biophysics, have enhanced our understanding of how motor proteins work. The horizontal integration component includes the immobilization of motor proteins on a microfluidic chip (which has its own vertical integration stream) for mechanical transduction, sorting, etc. This horizontal integration would not be viable unless there were sophisticated tools to characterize and manipulate motor proteins in non-biological environments, like single molecule imaging techniques, optical and magnetic tweezers, etc.

[2] Motor proteins are a broad class of biological molecules that enable movement along a substrate. The most well known motor protein is myosin, which enables muscular contraction.

An important feature in future nanotechnology prototypes is mimicking architecture and mechanisms from nature and existing structures to design more sophisticated structures. Drug delivery aims to build a synthetic virus- fusogenic peptide sequences mimicking the viral cellular penetration and pH sensitive intracellular drug delivery mimicking endosomal acidification (and activation) of viruses are being designed to improve the efficiency of drug delivery. The “Nanocar” is a supramolecule that mimics the wheel and chassis architecture of a car. This “mimetic” aspect of nanotechnology reinforces the concept of streams mentioned in the previous paragraph. Additional examples of biomimetic and technomimetic concepts are given in Table 1.



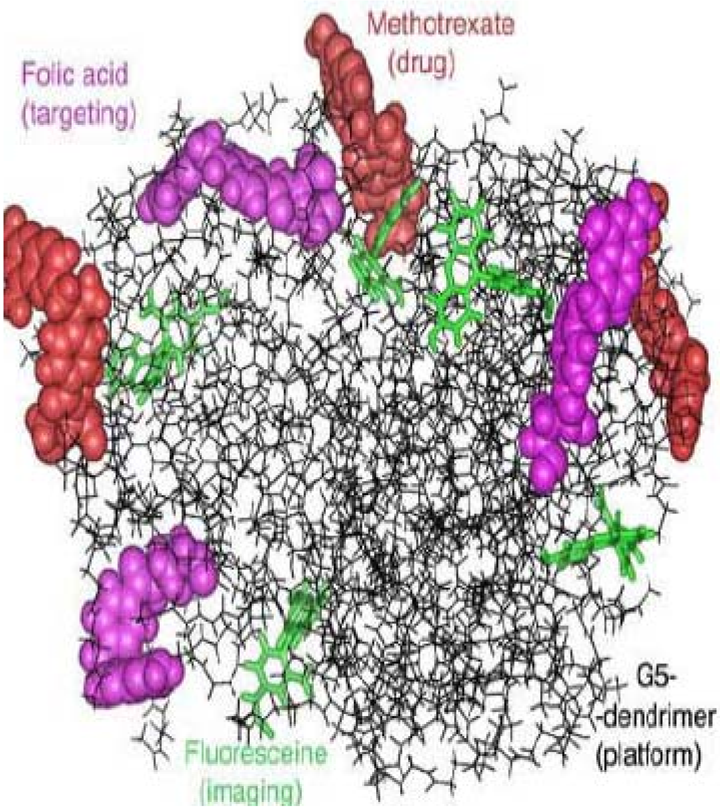
(Source: Rice University website)

TABLE 1 EXAMPLES OF BIOMIMETIC AND TECHNOMIMETIC CONCEPTS

BIOMIMETIC	TECHNOMIMETIC
Molecular Imprinted Polymers Artificial allosteric (receptor) systems	Molecular wheelbarrow Molecular gear

Artificial muscles	Molecular valve
"Virus" inspired drug delivery	Nanocar
	Nanotrucks
	Nanovalve
	Nanobearing
	Molecular turnstile
	Nanoimpeller

I have accepted the broadest conceptualization of active nanostructures in my work. Some active nanostructures in my dataset are a linear extension of earlier concepts, while others are novel. An example of the former is the multifunctional "Find-Detect-Treat" dendrimers platform, which integrates the formerly separate modalities of a targeting group, detection/imaging group and the drug. An example of a novel active nanostructure is a nanotube radio, which integrates the functions of an antenna, tunable bandpass filter, amplifier, and demodulator within a single carbon nanotube.



(Source: Kukowska-Latallo, Baker et al., Cancer Research, 65, 5317, 2005)

In prototypes with more than one active principle, the sequence of the active principles may also be of important. For example, polymers simultaneously responsive to temperature and pressure are distinct from photocommand surfaces, where the electric response of a surface to an external species depends on its photoisomeric state.

This exploration of the literature suggests that materials which have "bottom up" chemistries (e.g. polymers,supramolecules, peptides, etc) are thriving grounds for novel nanotechnologies. As expressed by others. I agree that prototypes that use fabrication techniques viable to economy of scale of production (various types of lithography, self assembly and a combination thereof) are more likely to be commercialized in the immediate future. For example, developments in hybrid silicon-organic electronics may occur before molecular electronics.

Active nanostructures are a broad concept, and a typology will be useful in advancing the discourse about them. Developing a typology about scientific research, particularly nanotechnology, is challenging because a) Scientists pursue their unique research interests, subject to the usual incentives of funding, peer reviewed publishing, etc. b) A typology is a simplification of the research; a good typology should retain the essential features of the research. c) Commonly used typologies were found to be "messy" and not useful to further the discussion of policy and oversight. Classification by material, technology or architecture yields too many categories and does not capture the salient features of the research. Classification by applications is messy because a single prototype (or slightly modified versions of it) is used for many applications. For example, similar polymeric encapsulation technologies are used for drug delivery in nanomedicine, nutrient delivery in agriculture and corrosion inhibitor delivery in anti-corrosion technology.

I suggest the following typology based on the basic categories *emerging from the research literature*.

1) Remote Actuated Active Nanostructure: I define "Remote Actuated Active Nanostructure" as nanotechnology whose active principle is remotely activated or sensed.
2) Environmentally Responsive Active Nanostructure: I define "Environmentally Responsive Active Nanostructure" as nanotechnology that is sensitive to stimuli like pH, temperature, light, oxidation-reduction, certain chemicals, etc.
3) Miniaturized Active Nanostructure: I define "Miniaturized Active Nanostructure" as nanotechnology which is a *conceptual* scaling down of larger devices and technologies to the nanoscale.

4) Hybrid Active Nanostructures: I define “Hybrid Active Nanostructures” as nanotechnology involving uncommon combinations (biotic-abiotic, organic-inorganic) of materials.
5) Transforming Active Nanostructures: I define “Transforming Active Nanostructures” as nanotechnology that changes *irreversibly* during some stage of its use or life.

It is important to note that active nanostructure prototypes are not meant to fall into exclusive categories. In fact, overlapping categories indicate greater complexity and dynamic behavior, either in an additive or synergistic manner, which should be considered in risk assessment. The active nanostructure research examples make explicit reference to the applicability of the typology. In the following section, we describe the frequently occurring research examples that fall *primarily* into each category. In addition, some of the research encountered does contain active principle(s), but is significantly more complex and dynamic, and often in the realm of basic stages of research. We describe them in the section 5.

4.1 Remote Actuated Active Nanostructure

Remote actuated active nanostructures include magnetic, electrical, light and wireless tagged nanotechnologies. These technologies utilize parts of the electromagnetic spectrum [3] for activation, sensing and communications. Nanotechnology has enabled us to use more regions of the electromagnetic spectrum, and in unique devices.

The integration of the sensing with a wireless modality is important in embedded sensors for biomedical, environmental, agricultural and surveillance applications. For example, one sensor uses tin

[3] The **electromagnetic (EM) spectrum** is the range of all possible electromagnetic radiation, including radio, microwave, infra-red, visible, ultraviolet, X-rays and gamma rays.

oxide nanoparticles has been integrated with a patch antenna for wireless detection of ethylene gas emitted from over-ripened fruits. Similarly, actuation and drug delivery may be coupled with the wireless modality.

Light is one of the most important "remote actuators" in the active nanotechnology literature. An innovative active nanostructure based on light is the artificial light harvesting antenna, which mimics its analogue in photosynthetic plants and microorganisms. The basic concept involves a light sensitive species, which absorbs light and gets excited, and transfers this energy to other species. Artificial light harvesting antenna may be used in solar energy conversion devices. Nanotechnology has also continued the progress in "active layers" based on photovoltaic phenomena and room temperature photoluminescence and, which can be applied sensors, catalysts and solar cells. Optoelectronics provides materials for telecommunication, information processing, and radars. Plasmonics[4] is also a thriving area for sensors based on spectroscopic signatures and optical data transfer.

High frequency (gigahertz or terahertz) oscillators based on fullerenes and carbon nanotubes are also an active area of research that will yield nano-antennae for wireless applications.

4.2 Environmentally Responsive Active Nanostructure

An environmentally responsive active nanostructure is one which undergoes its change of state in response to a specific environmental cue. Examples of environmentally responsive active nanostructures include sensors, light driven molecular motor, responsive drug delivery, environmentally responsive actuators,etc.

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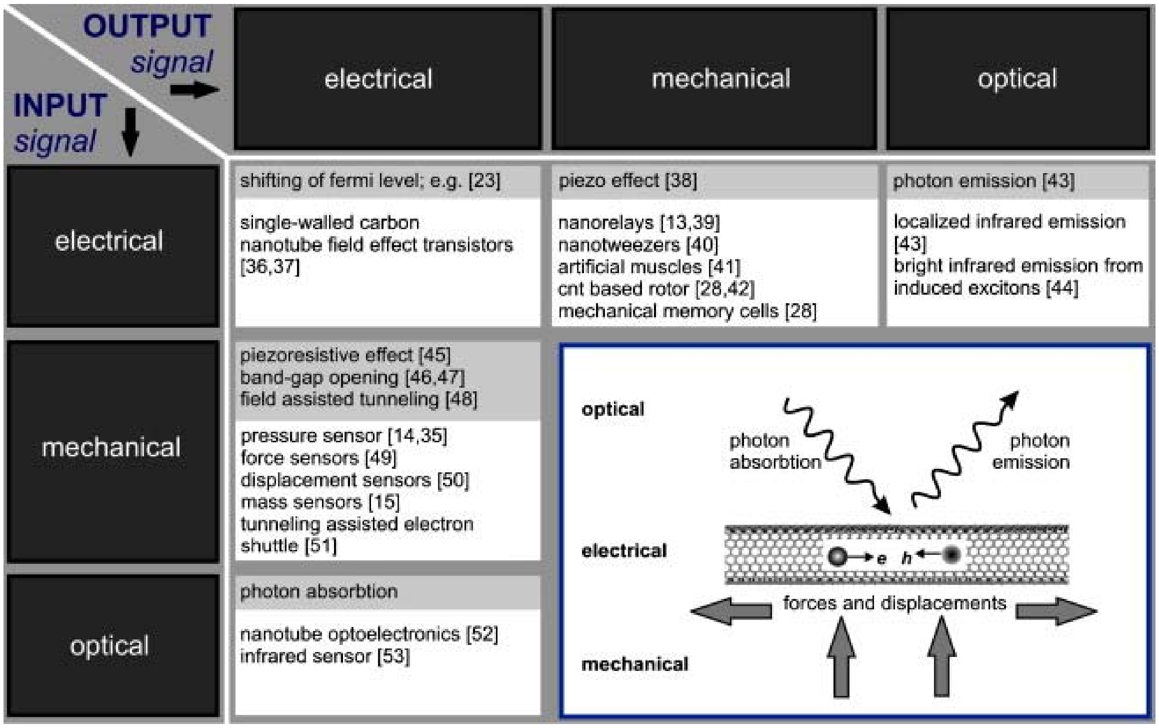
[4] Plasmons are density waves of electrons, created when light hits the surface of a metal under precise circumstances.

4.2.1 Sensors

Sensors are one of the most thriving areas of active nanostructures research in the literature. In this document, the term “sensor” is broadly construed as any in vitro, in vivo or device based stimuli detection at the nanoscale. Detection principles enabled by nanotechnology are numerous: electrochemical, acoustic, optical, mechanical, etc.

An important distinction to be made about many sensors categorized as active nanostructures is that they are “label-free” (as opposed to label based), and sense changes in intrinsic properties of the sensing interface due to the presence of the analyte. For example, a biosensor based on magnetoelastic materials senses the binding of a bacterium (analyte of interest) with a bacteriophage (recognition element on the sensor) as a change in the resonant frequency. Some other examples are illustrated in the table below, which shows the NEMS sensors based on carbon nanotubes. The rows of this matrix illustrate the “input” signal (or the stimulus), and the columns of the matrix illustrate the “output” signal (or the response). The columns in the cells in the grey background specify the nanoscale phenomenon associated with the given input and output signal.



Source : Helbling et al (2007) "Nano electromechanical sensors based on carbon nanotubes "

The transduction principle may also enable integration of previously distinct components of the sensor architecture. For example, nanowires and carbon nanotubes often integrate the sensing and electrical interface of sensor devices. Detection can also be based on more than one criterion. For example, a molecular imprinted polymer [5]with an "enzyme sensitive groove" mimics the enzyme-substrate "lock and key" interaction in biology- detection is based on a structural fit as well as chemical detection.

Higher surface areas of nanostructures provide an increased sensing area, and some nanoscale sensors tout a "near molecular scale" detection limit. This higher sensitivity translates into the redundancy of a pre-analysis step (e.g. Amplifying microbial DNA using Polymerase Chain Reaction (PCR) for detecting

[5] A **molecular imprinted polymer** is formed in the presence of a molecule that is extracted afterwards, thus leaving complementary cavities behind. These polymers show some affinity for the original molecule and can be used to fabricate sensors and catalysts.

microorganisms, Preconcentration step for gas/explosives detection) and viable diagnostics in matrices with low analyte concentration (Example salivary biodiagnostics). The miniaturization of sensors to portable devices will also enable personal health monitoring and point of care diagnostics. The research literature also shows viable sensors for detection of proteins, which has been difficult in the past.

Active nanostructure based sensors are also improving manipulation tools by providing sensing probes for piezoresistive cantilever structures in microscopy. For example, molecular absorption of an analyte on a probe functionalized with nitrogen rich carbon nitride film can be sensed as a change in stiffness of piezoresistive cantilever. Similarly probes for sensing temperature and other chemical and biological stimuli have also been designed.

Improvements in nanoelectronics and artificial intelligence are also improving stochastic sensors[6] such as electronic nose and electronic tongue. These systems mimic the human olfactory and taste receptors to sense various odors and flavors respectively. They comprise of a reactive element array and a computing system which uses pattern recognition algorithms to provide an electronic signature of the analyte. Nanowires, carbon nanotubes, surface acoustic wave sensors and field effect transistors provide more sensitive array platforms for these sensors.

4.2.2 Actuators

An actuator [7] is used in microfluidic chips and other devices to achieve functions like specific movements, movement of "cargo" and sorting. Materials making up composites include sol gels, ionic polymer metal composites, carbon nanotube-polymer composites, deformable polymer based systems

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[6] **Stochastic sensors** are characterized by randomness and use pattern recognition algorithms to detect the presence and concentration of an analyte.

[7] An **actuator** converts a stimuli or any form of energy into mechanical motion.

(like dielectric elastomers , liquid crystal elastomers, ferroelectric polymers, conducting polymers, etc.), thermal and ferroelectric shape memory alloys, biological components like microtubules and (biological) molecular motors, magnetoelastic materials and supramolecules. Actuators are a class of active nanotechnology that will be incorporated into finished products.

4.2.3 Environmentally sensitive Drug delivery

Environmentally sensitive drug delivery includes carrier designs that are sensitive to local microenvironments like pH, temperature, enzyme, ionic strength, redox etc. Design of an environmentally sensitive drug delivery system often makes use of a physiological environment (including a pathological state) that provides the “stimulus” for the functionality. For example, tumors have a higher temperature (by 2-5 degree Celsius) and lower pH (by 0.5-2.5 units) than the rest of the body and this may be used to design carriers to deliver anti-cancer drugs to the tumor site. A carrier of peptide based drugs has been used to remain inert in the stomach and release the peptide in the intestine, making use of the pH difference between these organs. Environmentally sensitive drug delivery can greatly enhance delivery efficiency of therapeutic molecules like drugs, genes and polypeptides (e.g. insulin, small interference RNA, peptide nucleic acids, etc.), and also reduce the side effects due to incidental interactions. Sensitivity to more than one stimulus has also been achieved with block copolymers[8].

Various types of carrier morphologies have been used to facilitate pH responsive drug delivery including liposomes, micelles, dendrimers, core shell structures and other polymeric nanocarriers. Their design involves disruption of the therapeutic-carrier complex (phase transition, bond cleavage, carrier

[8] **Block copolymers** are formed by the sequential addition of two or more monomer subunits (“blocks”) linked by covalent bonds. Block copolymers with two or three distinct blocks are called **diblock copolymers** and **triblock copolymers**, respectively. Each block can have sensitivity to a certain stimulus.

dissolution, etc.) in response to the microenvironment pH, and makes the therapeutic dose available for uptake.

Temperature sensitive drug delivery utilizes thermosensitive polymers or copolymers to release

To treat cancer, temperature sensitive drug delivery may also be advantageously combined with hyperthermia[9] therapy of the tumor mass.

The difference between the redox conditions in extracellular and intracellular environments is another stimulus that can be targeted by environmentally responsive drug delivery. For example, glutathione [10] inside the cells are at concentrations hundred to thousand-fold greater than the extracellular environment. Drug delivery designs based on polymeric carriers and liposomes incorporate the reduction of the disulfide bond by glutathione as a basis for making the therapeutic dose available for uptake. Redox based cell signaling is also being elucidated in many diseased states, and redox sensitive drug delivery may also be used to “intercept” dysfunctional signaling.

4.3 Hybrid Active Nanostructures

Hybrid active nanostructures are one of the most novel categories that emerge from the research and includes a combination of organic and inorganic materials. Two classes that will be discussed here are biotic-abiotic hybrid and silicon-organic hybrid nanostructures.

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[9] **Hyperthermia** can be used for cancer treatment by exposing the tumor tissue to high temperatures to kill the cancer cells and shrink tumors.

[10] **Glutathione** is a tripeptide that is a constituent of all living cells and protects cells from oxidants such as free radicals.

4.3.1 Biotic-Abiotic

A biotic-abiotic hybrid device is one that mobilizes biological nanoscale components like DNA, protein, membrane, membrane channel pore, photosystem, enzymes, and cofactors in an abiotic environment to perform an active function. It is important to reiterate the latter part of this definition: the novelty of a biotic-abiotic hybrid device is not just due to the unusual combination of materials, but also the active functionality. Many biological assays involve the mobilization of enzymes and antibodies on surface, and may also have a detection function (e.g. ELISA[11]) - but they are not biotic-abiotic active nanostructures. However, an enzyme responsive hydrogel, comprising of an oxidoreductase enzyme[12] immobilized in a three dimensional polymer network which shrinks on enzyme catalysis is a biotic-abiotic active nanostructure. The possibility of "engineering" living systems is novel.

The general advantages to using biological components in hybrid devices are: a) Elegant and fault tolerant architecture (including self assembly) b) Abundant availability c) Possibility of self replication d) Already present functionality.

Motor proteins or whole organisms containing functional motor proteins can be tethered to surfaces to produce linear and rotary motions (that they produce in living systems) in hybrid devices. Examples of rotary motors include F_1F_0- ATP synthase, *Mycoplasma mobile* (bacteria) and bacterial flagellar motor, and those of linear motors include myosin, kinesin, dynein, DNA polymerase and RNA polymerase. Motor proteins can be processive, or perform the desired motion many times or non-processive. They

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[11] **ELISA,** acronym for **Enzyme-Linked ImmunoSorbent Assay**, is a widely used technique to detect the presence of an antigen in a sample by using its complementary antibody.

[12] **Oxidoreductase** enzymes catalyzes the transfer of electrons from one molecule (the reductant) to another (the oxidant). Examples include glucose oxidase, lactose oxidase, alcohol oxidase, etc.

function by various mechanisms, such as substrate binding, redox reactions, ionic and pH gradients, and are mostly powered by the fuel ATP.

Motor like functionality can also be achieved with biological constructs composed of DNA, RNA, ribosome, etc. For example, autonomously moving DNA motors powered by DNA fuels and hybridization with complementary strands have been designed. Biological membranes tethered on abiotic supports with active components are another area of growing research.

4.3.2 Silicon Organic hybrid nanotechnology

Silicon-organic hybrid nanotechnology represent a class of materials, mainly in electronics, where traditional silicon-chip technology is coupled a nanoscale organic components (e.g. a film) to obtain a hybrid device. Silicon-organic hybrid nanotechnology may be a prelude to molecular electronics as these devices can be fabricated by a combination of lithography and existing techniques of self assembly. Some of the materials being used in this area include carbon nanotubes, carbon and silicon nanowires , organic polymers and supramolecules.

4.4 Miniaturized Active Nanostructure

Miniaturized active nanostructures involve a conceptual scaling down of larger technologies and devices, and are a thriving area for many technomimetic architectures and bottom-up construction. They include assemblies of functional molecules which can perform specified functions, based on phenomena such as redox, isomerization, chirality light activated phenomena, etc. These phenomena are not novel and have been observed in solutions for a long time, but the most useful applications of nanotechnology in molecular machines require them to be expressed on a surface (eg film, monolayer etc.) or a three dimensional structure (eg gel). The applications include informational (e.g. logic gate), electronic (e.g. single electron transistor) and mechanical (eg molecular motor). Examples include synthetic molecular motors, molecular machines and molecular electronics structures.

Miniaturization to the nanoscale has unique implications that are complex, but non-scientists need to understand at a basic level. Scaling down from a Newtonian to Quantum mechanics framework implies a higher role for uncertainty in these systems. An illustration is Brownian motion[13] , which is significant at the nanoscale. It is a law of nature that all objects try to achieve thermodynamic equilibrium with a tendency to go to a state of lowest energy. While macro-scale objects appear to be "in equilibrium", the achievement of equilibrium is a *continuous process* at nano and smaller scales, where it is characterized by *random and small energy fluctuations tending towards equilibrium*. Synthetic molecular machines and other miniature active nanostructures harness such random and small energy fluctuations to generate controllable processes.

Many synthetic molecular motors are based on supramolecules[14]. These include molecules like cyclodextrin [15] and cyclophanes[16] as well as mechanically-interlocked molecular architectures like rotaxanes, pseudorotaxane and catenanes. Mechanical interlocked molecular architectures will be discussed in detail to illustrate the interaction between individual functional molecules and architecture.

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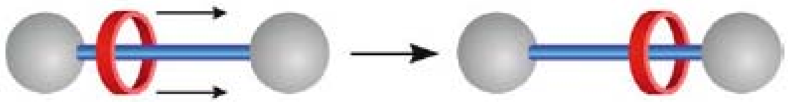
[13] **Brownian motion** is the random movement of particles suspended in a liquid or gas

[14] **Supramolecules** are two or more molecules held together by intermolecular (noncovalent) interactions. Non covalent interactions are weaker and reversible, and form the basis of concepts such as molecular self-assembly, folding, molecular recognition, host-guest chemistry, mechanically-interlocked molecular architectures, and dynamic covalent chemistry.

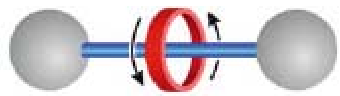
[15] **Cyclodextrins** are (artificial) cyclical compounds with six to eight sugar molecules.

[16] C**yclophane** consist of a aromatic (ring) unit and a chain unit that forms a bridge between two non-adjacent positions of the ring.

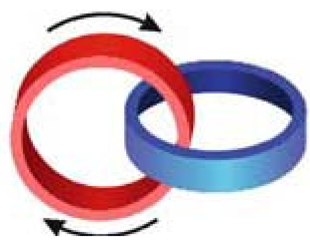
Rotaxane (Latin: *rota*- wheel, *axis*- axle) is a molecular architecture comprising of a macrocyclic molecule ("wheel") threaded through a dumbbell-shaped molecule ("axle"). The ends of the dumbbell in a rotaxane are terminated with bulky groups ("stopper") to prevent disassembly. In the case of pseudorotaxanes the bulky groups are absent and the "wheel-on-axle" complex can be dissociated. Catenane (Latin: *Catena*-chain) is a molecular architecture comprising of two interlocked macrocycles. Recently, catenanes with three interlocked macrocycles have also been obtained. By appropriate selection of the wheel, axle and stopper molecules, architectures that respond to specific stimuli (pH, electrochemical, light) in an attempt to reach lowest energy state have been designed. The rotaxane architecture lends itself to two inter-component motions: translation of the wheel on the axle and the rotation of the wheel about the axle. The catenane architecture lends itself to ring rotation. These are illustrated in the figure below.



Translation of the wheel on the axle in a rotaxane



Rotation of the wheel about the axle in a rotaxane



Ring rotation in a catenane

(***Source : Balzani V, Credi A, Ferrer B, et al. (2005) "Artificial molecular motors and machines: Design principles and prototype systems"***)

By designing two recognition sites ("stations") on the axle molecule, bistable rotaxanes can be obtained- where an external stimulus like pH, electrical field, oxidation/reduction and light causes a reversible switch from one state to another. The most obvious application of this molecular switch is a binary logic gate. Identical stations also provide for rapid molecular shuttling with pH, oxidation /reduction and light, providing the ability to transport molecules and ions. Molecular shuttling with rotaxane molecules has already been incorporated into active nanostructures for drug delivery –as impellers and valves to seal drug containing mesoporous silica nanoreactors, and release the drug in response to pH. A redox controlled "artificial muscle" Nanoelectromechanical System (NEMS) device has been demonstrated by forming a self assembled monolayer of a rotaxane based molecule on the gold surface of an array of microcantilever beams. Combination of a photosensitizer like Ruthenium (II) polypyridine with a rotaxane system or with a pseudorotaxane system enables the formation of an autonomous light-fueled molecular motor, where light can induce mechanical movements without the formation of waste products.

The ability to control ring rotation gives rise to useful catenane structures. Like rotaxanes, recognition sites ("stations") can be designed onto the macrocycles to obtain bistable catenanes, making it a potential molecular switch. An AND gate logic was shown by catenane $8H^{5+}$ by a switch in the position of the crown ether ring by a change in pH and redox.

Molecular electronics is being hailed as the enabler who will allow integrated circuits to continue to keep up with the Moore's Law[17]. Molecular electronics uses molecules like organic molecules, bimolecules, etc. (and collections thereof) to form building blocks of circuits. Many simple structures like transistors, rectifiers, diode, amplifiers, wires, switches, gates, magnets, etc have been built. Scientists are striving for better position, interface and property control, as well as compatible architectures. Development and commercialization of molecular electronics will require new techniques of fabrication.

4.5 Transforming Active Nanostructures

Transforming active nanostructures change irreversibly during its life cycle, and thus require risk analysis before, during and after the transformation. Many examples mentioned until now transform irreversibly; usually at the end of their life. This category also includes adaptive structures which transform irreversibly.

Self healing materials are an example of active nanostructures that almost always transform irreversibly. Self healing materials include metal and plastic coatings which on specific triggers, repair damage

[17] **Moore's Law**, postulated by Gordon Moore of Intel in a 1965 paper, predicts that the number of transistors that can be placed on an Integrated Circuit will exponentially double every two years.

caused by corrosion, mechanical damage, etc. Common architectures of self-healing materials include composite passive-active layered structures and nanoscale containers with active (repair) chemicals in a passive matrix. Often, repair is initiated with a stimulus trigger like crack (or deformation), light, pH, etc. Varying thermal and electrical properties at the defect may also be used as the stimulus to initiate repair, and facilitate “controlled” release of repair chemicals.

5. Conclusions

This exploration of research literature on active nanostructures raises more questions than it answers. But it is hoped that it helps the reader better understand emerging applications. It is also hoped that it will stimulate research about the implications of these emerging applications on oversight.

The Project on Emerging Nanotechnologies (PEN) is interested in the broader issue of the implications of nanotechnology on Science and Technology (S&T) oversight. This paper describes research that may yield prototypes that complicate risk assessment. For example, environmentally sensitive drug delivery is likely to be used for in vivo applications and requires a thorough consideration the transport and fate of the drug delivery system in the body. Stimuli like temperature and pH are “generic” and vary considerably in the body and it must be ensured that unintended interactions do not occur. The fate of the carrier after drug delivery, i.e whether it is excreted from the body (as hoped) or it concentrates in certain parts of the body is also a concern. The paradigms of toxicology have to be thoughtfully applied, particularly the notion of “biocompatibility”. In other words, it is not sufficient to say that a certain material does not cause an adverse reaction, what are the ramifications of putting it into a system where it would not go under “the usual circumstances”? These criteria are not used in current risk assessments. Analogously, the life cycle issues of nanomaterials in a prototype are important; whether they dispersive or bound to a matrix or how they are eventually disposed.

Many prototypes in the categories of hybrid active nanostructures and transforming active nanostructures are of particular interest to risk assessment because of the life cycle issues associated with them. Consider the implications of a biological motor on a diagnostic chip. How is it immobilized on the chip? Will it require special disposal? Life cycle issues with transforming active nanostructures can also be challenging.

Another important consideration is the processes by which these prototypes will be produced, and its implications. Is the production process economically viable? Does it need new industrial infrastructure and production techniques? Will it destroy existing industries, or merge with them? These considerations are voiced in literatures dealing with conventional and molecular electronics.

These examples are some suggestions of the oversight considerations arising from emerging applications of nanotechnology. An exhaustive and systematic evaluation of oversight implications, particularly before they enter the regulatory pipeline will be useful.

Appendix 1 Preliminary search terms

NEMS, nano* AND active, nano* AND sens*, nano* AND smart, nano* AND feedback, nano* AND molecular, nano* AND stimuli responsive, nano* AND corrosion protection, nano* AND electronic nose, nano* AND self healing, nano* AND shuttle, PEBBLES, nanorobots, artificial muscles, nanoactuator, nanobarcode, nanobearing, nanovalve, nanodevice, nanogap capacitor, nanogear, nanopore, viral protein cage, AFM tip And sens*, fullerene AND active, fullerene AND intelligent, rotaxane AND nano*, Rotaxane AND motor, Catenane AND nano* and Catenane AND motor

Appendix 2 About Vantage Point

VantagePoint works with search results from text databases. First conduct a search using a search engine provided by your database provider. Then download the raw data to your computer, and import it into VantagePoint using an Import Filter.

VantagePoint is most useful when your search strategy returns "more than you want to read." It can provide great benefit when working with only a few dozen records, but it is most helpful when you need to work with thousands of records.

From http://www.thevantagepoint.com/vantagepoint.cfm

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