Gold Nanoparticals for biomedical applications

Akbar Vaseghi *Dr. Babak Bakhshinejd* *Prof .Majide Sadeghizade* *Reza Ashrafi Parchin*

Department of Genetics and NanoBiotechnology, Faculty of Biological Sciences, Tarbiat Modares University , Tehran, Iran

Young Researcher Club, Science and Researcher Branch,Islamic Azad University, Ardabil, Iran

➢Outline

➢**Introduction:**

❖ **Nano-Biotechnology**

➢**Gold Nano-particles:**

❖**Diagnosis and Imaging (bacterial detection)**

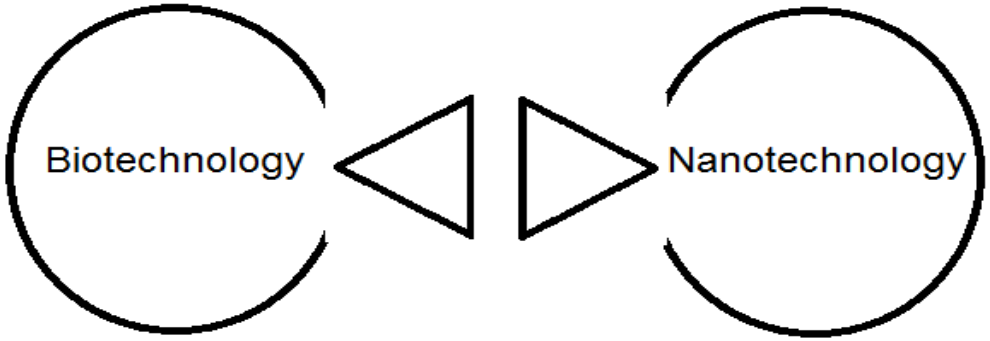
❖**Therapeutics (drug delivery)**

➢**Discussion and Conclusion**

➢Nano-Biotechnology

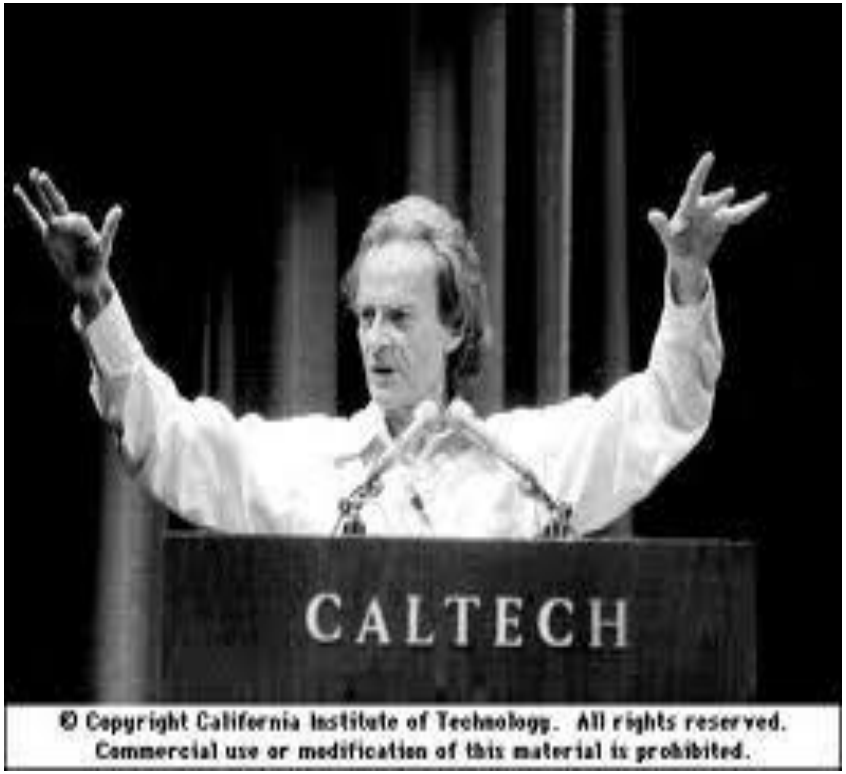
❑ *Three novel Technologies* : **Biotechnology, Nanotechnology Information technology**

❑***Nanobiotechnology*** *is* the crossroads of ***biotechnology*** and ***nanoscience***



❖Often considered one of the key technologies of the 21st century.

❖Many important applications in extents such as medical, agricultural biotechnology and food industry

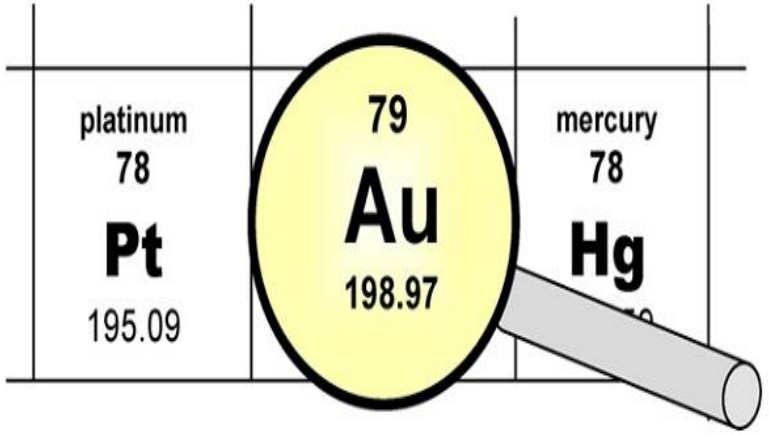


The origins of foucused reserch in to nanostructured materials can be traced back to a seminal lecture give by Richard Feyman in 1959 and DR. CHAD A. MIRKIN 1996

➢Gold Nano Probes (AuNPs)

History:

$$[Xe]4f^{14}5d^{10}6s^{1}$$



➢The use of gold for medicinal dates back to 2,500 BC to the ancient Chinese and Egyptian

➢In medieval Europe, numerous recipes for gold elixirs existed and in the 17th and 19th century gold was used to treat fevers and syphilis respectively

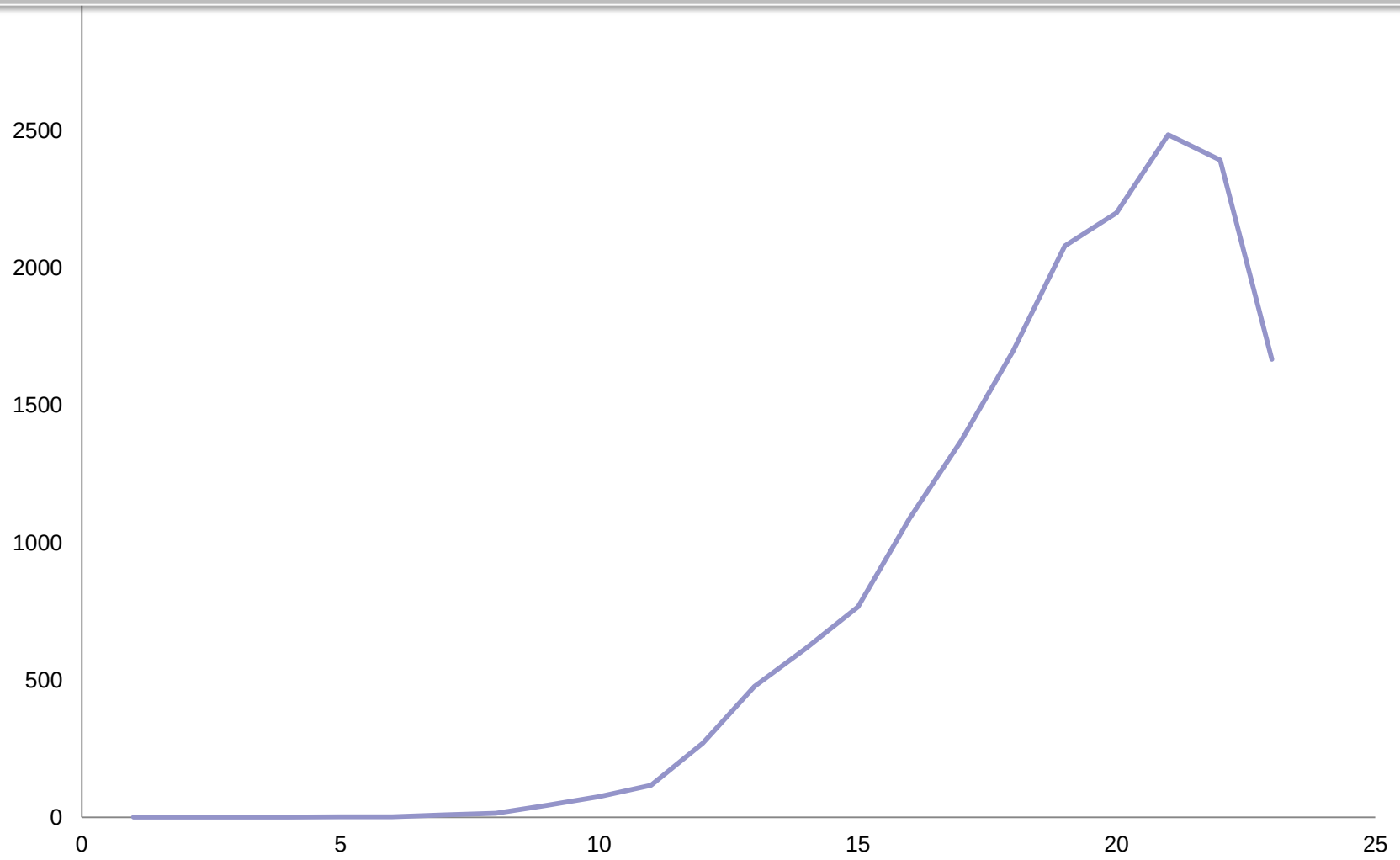
➢The use of gold in modern medicine began in 1890 when the German bacteriologist Robert Koch discovered that gold cyanide was bacteriostatic to the tubercle bacillus in vitro

➢As RA was initially thought to be an atypical form of tuberculosis, Laude used gold to treat RA in 1927

➢Used as a therapeutic agent to treat a wide variety of rheumatic diseases including psoriatic arthritis.

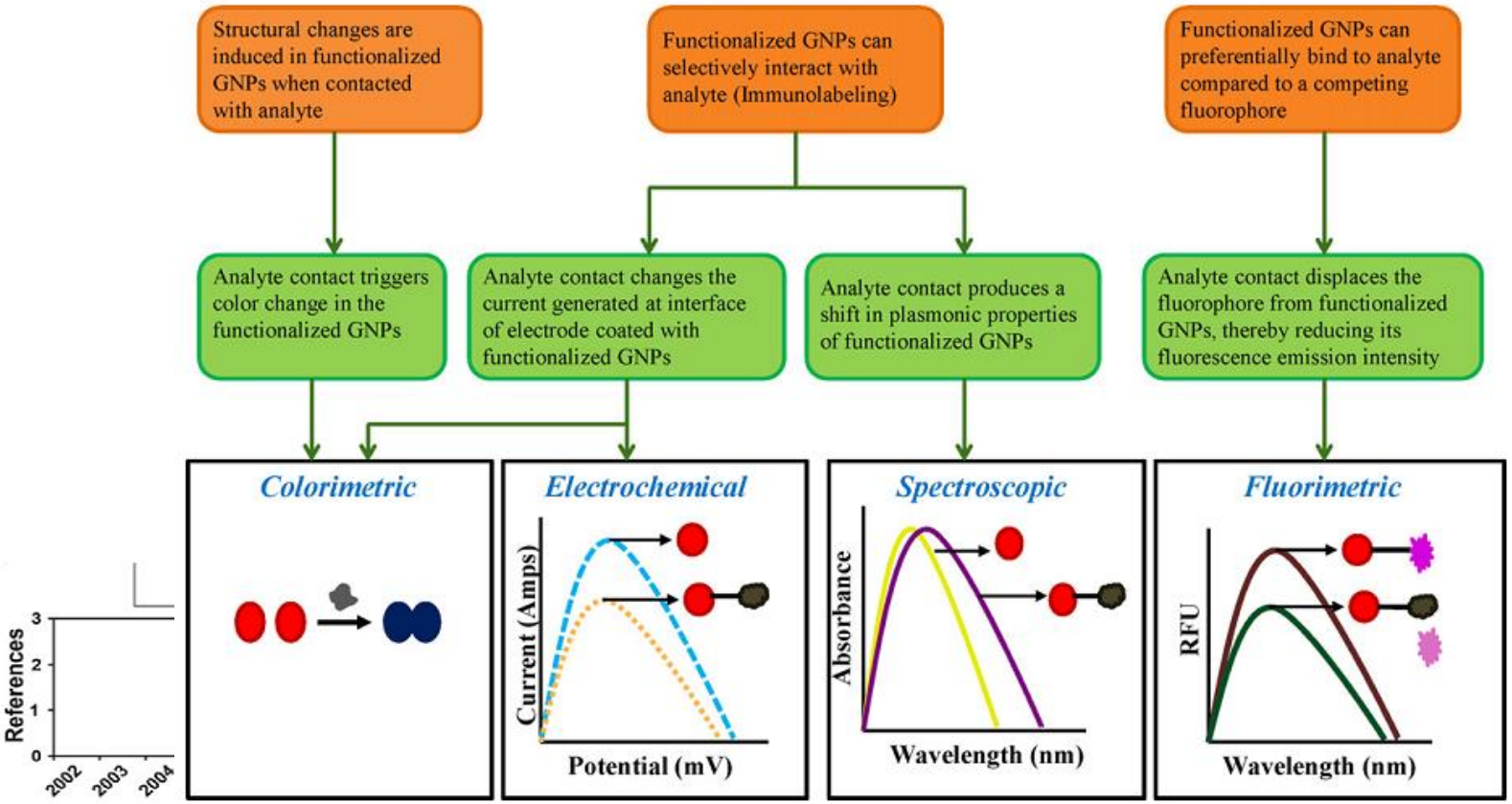
➢ Juvenile arthritis and discoid lupus erythematosus

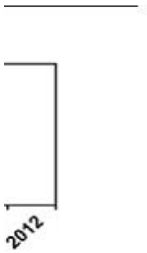
➢Gold Nano particles (AuNPs)

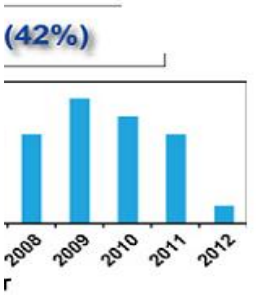


Gold nano-particles 17396

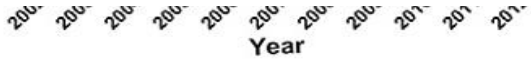
➢Gold Nano particles (AuNPs)



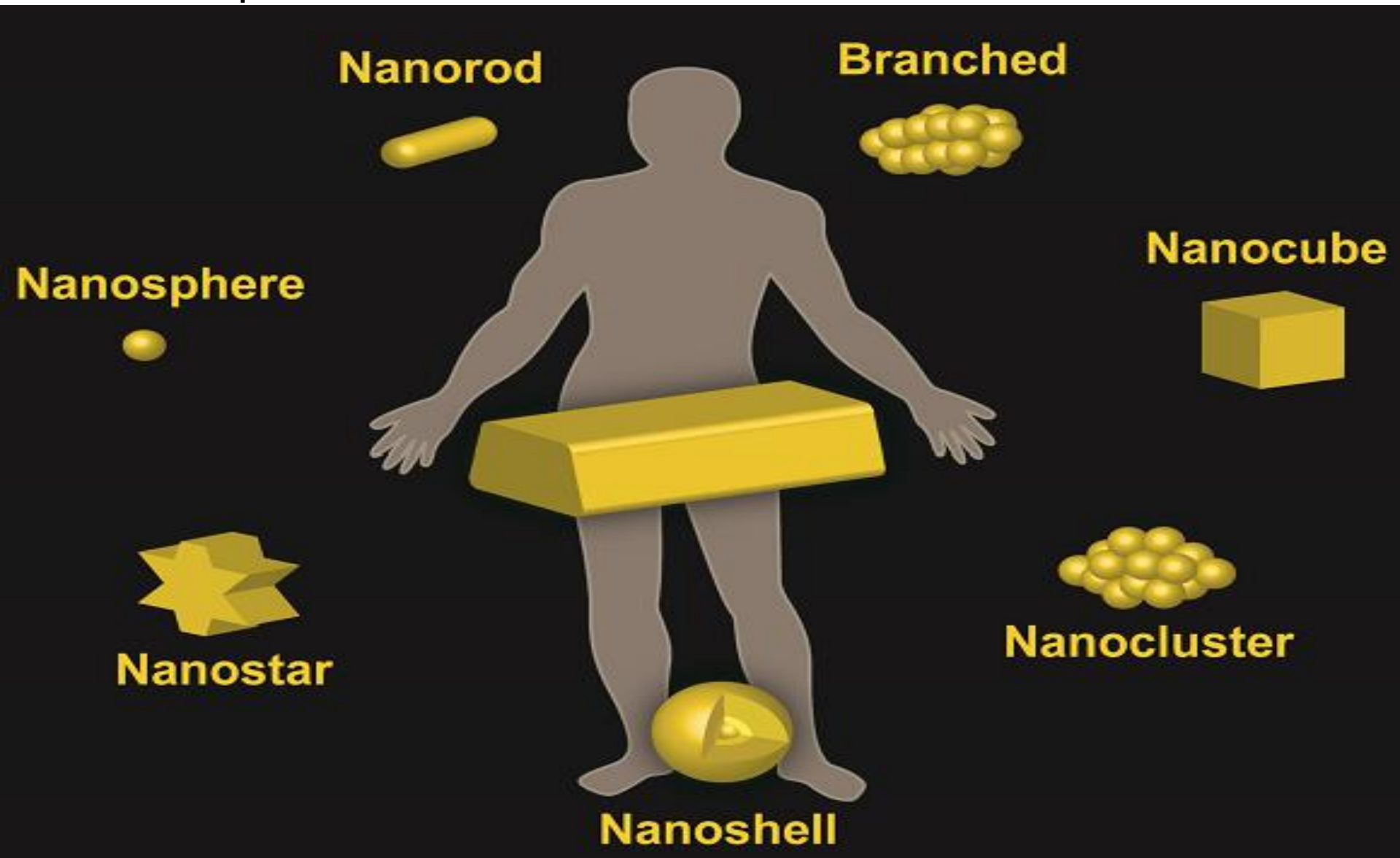




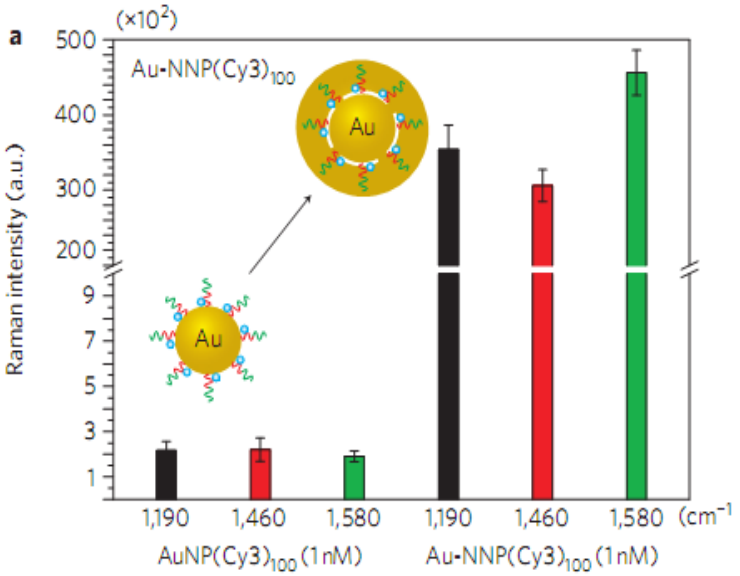
Schematic of GNP functionalization schemes and detection mechanisms applied in detection chemical and biological threat agents

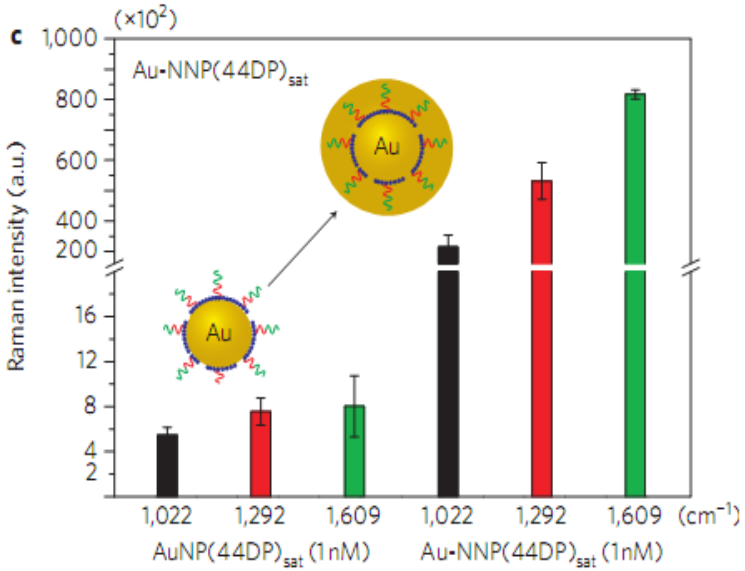


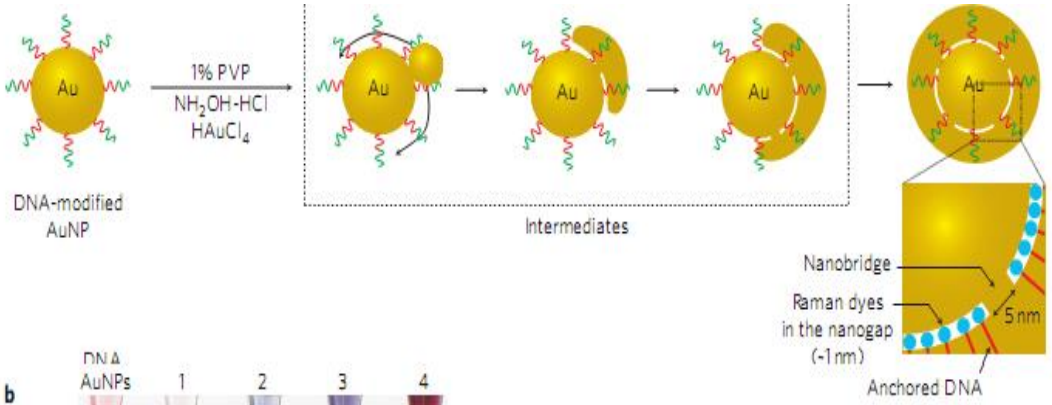
Schematic representations of gold nanoparticles use… clinical practice

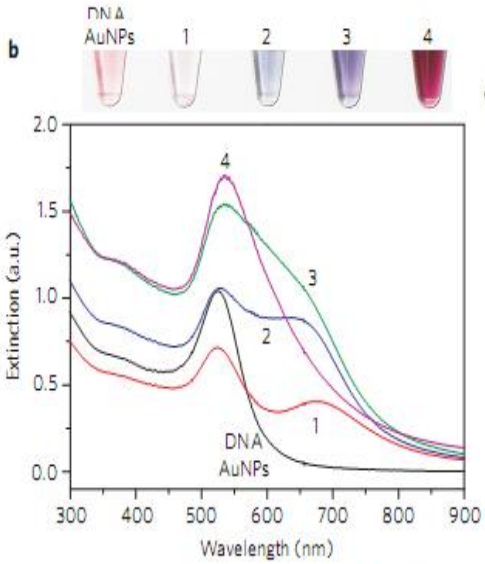


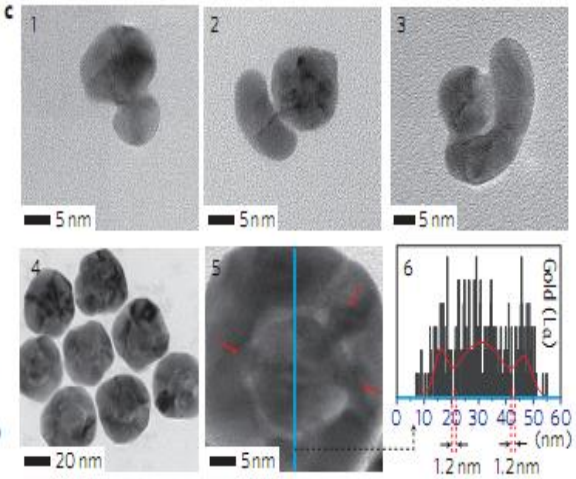
DNA -anchored Nano brideged Nanogap particles (Au-NNPs)

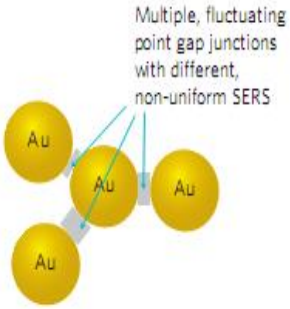


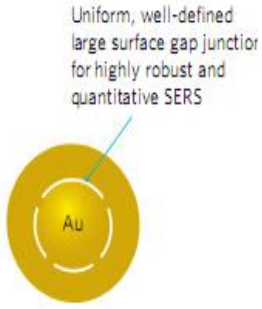












➢Gold Nano- Probes

Gold nanoparticles (AuNPs) are the most extensively investigated nanomaterials, due to their distinct physical and chemical attributes, as follows:

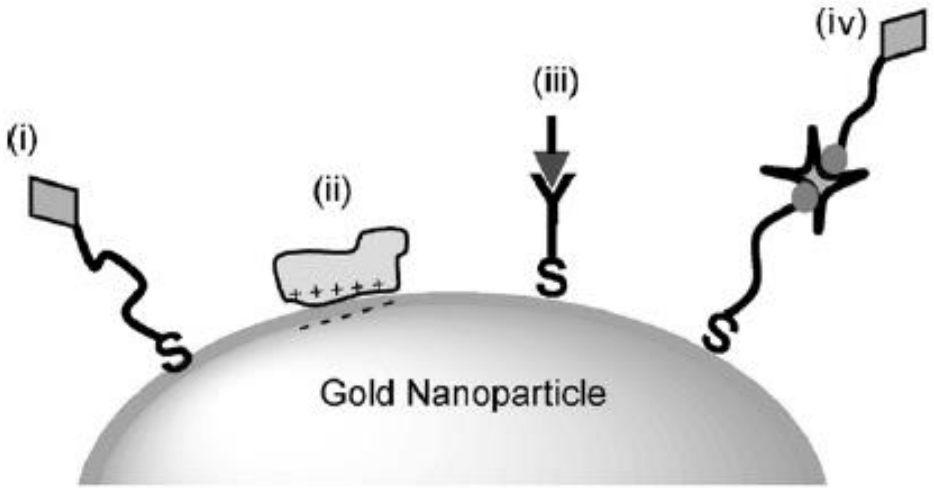
✓It is easy to synthesize stable AuNPs.

✓ AuNPs possess unique, tunable optical properties (Quantum confinement).

✓ AuNPs provide a high surface-to-volume ratio (5nm 20 % and 1 nm 100%).

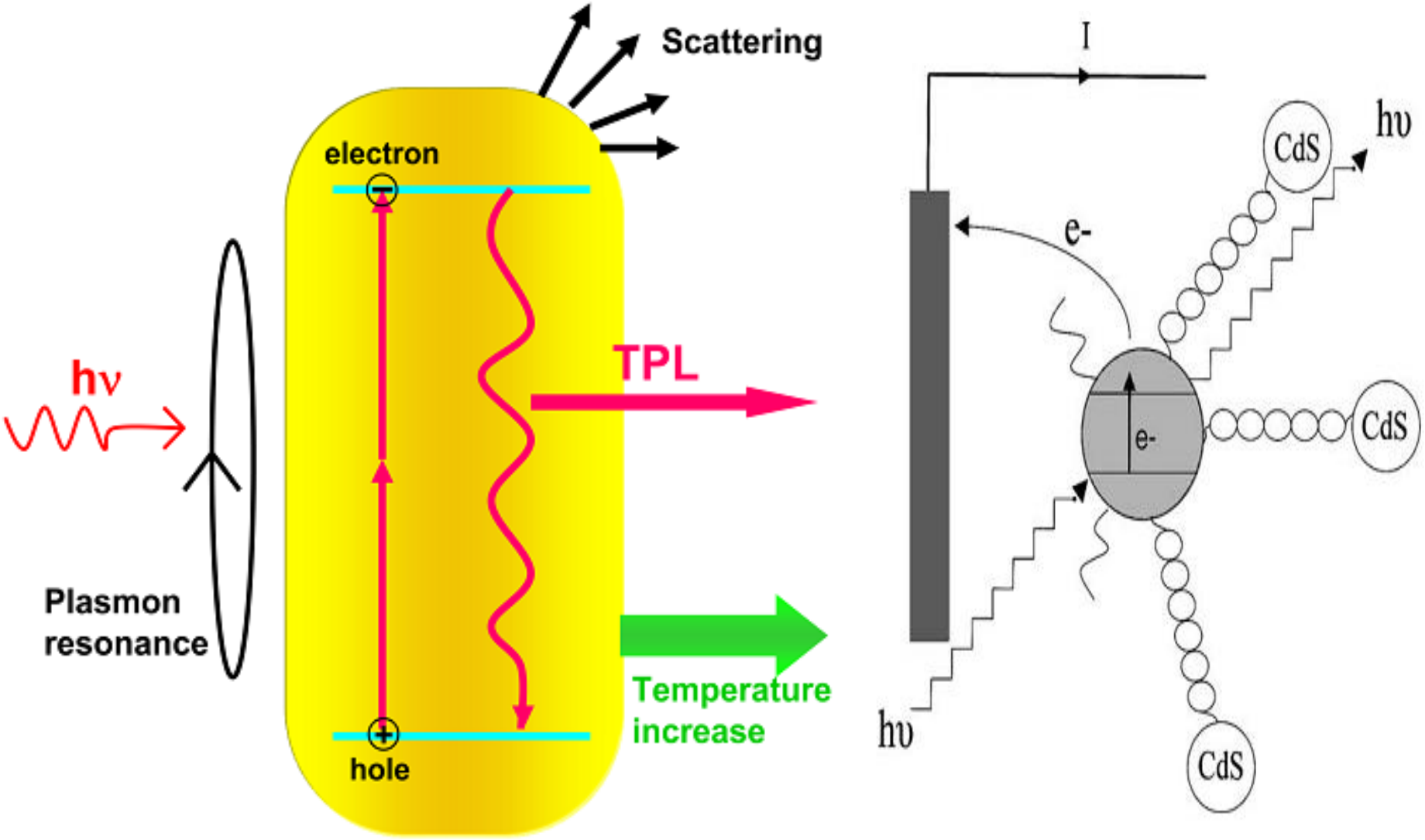
✓ AuNPs exhibit excellent biocompatibility after appropriate modification.

✓ AuNPs offer a platform for functionalization with ligands for the specific sensing of targets.



(i): thiolated or disulfide modified ligands
(ii):Electrostatic interaction
(iii):antibody–antigen associations
(iv):streptavidin–biotin binding

Photophysical processes in gold NRs



➢Gold Nanoparticle (AuNPs)

❖**Applications of gold nanoparticle probes:**

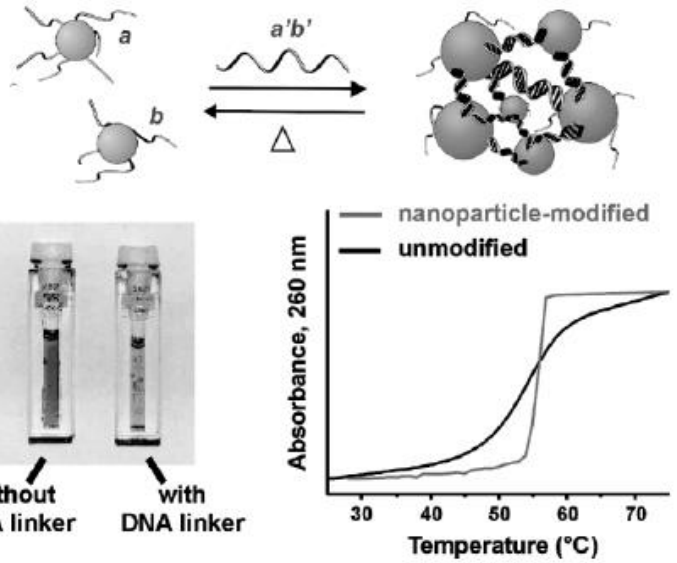
- ➢Nanobiosensor
- ➢Diagnosis and treatment of diseases
- ➢Identification and treatment of cancer
- ➢Drug and gene delivery
- ➢Production of nanowier
- ➢Genetic analysis
- ➢Virus study
- ➢Cell structure study
- ➢Gene transfer in plants
- ➢Increase resolution of MRI,CT and X-ray imaging
- ➢Detection of Pb_{2+}, Cr_{2+} and TNT
- ➢ and so on ……

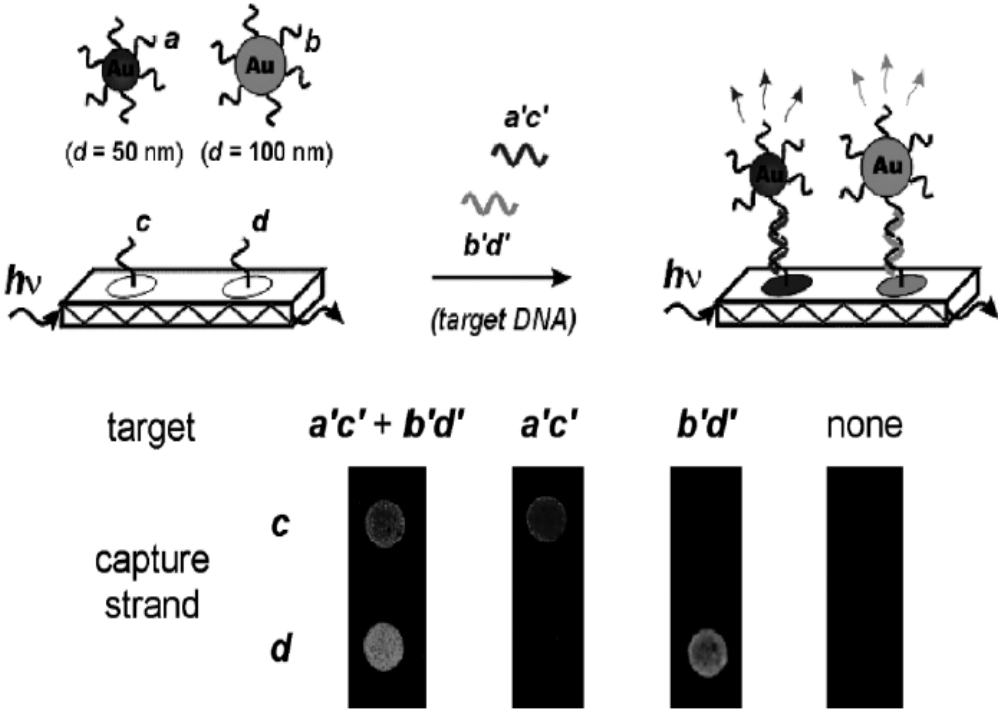
➢Gold Nanoparticle Probes (AuNPs)

Nanoparticle Based DNA and RNA Detection Assays:

❑Homogeneous DNA Detection:

In 1996, Mirkin and co-workers reported the use of mercaptoalkyloligonucleotide-modified gold nanoparticle probes (DNA–Au-NP probes) for the colorimetric detection of cDNA target sequences *(Mirkin, C. A., et al. 1996)* .





Mirkin, C. A., et al. *A DNA-based method for rationally assembling nanoparticles into macroscopic materials. Nature* ***1996****, 382, 607–609*

➢colorimetric detection

➢Gold Nanoparticle (AuNPs) probes for colorimetric detection.

amplification of a genomic region

▼

hybridization

▼

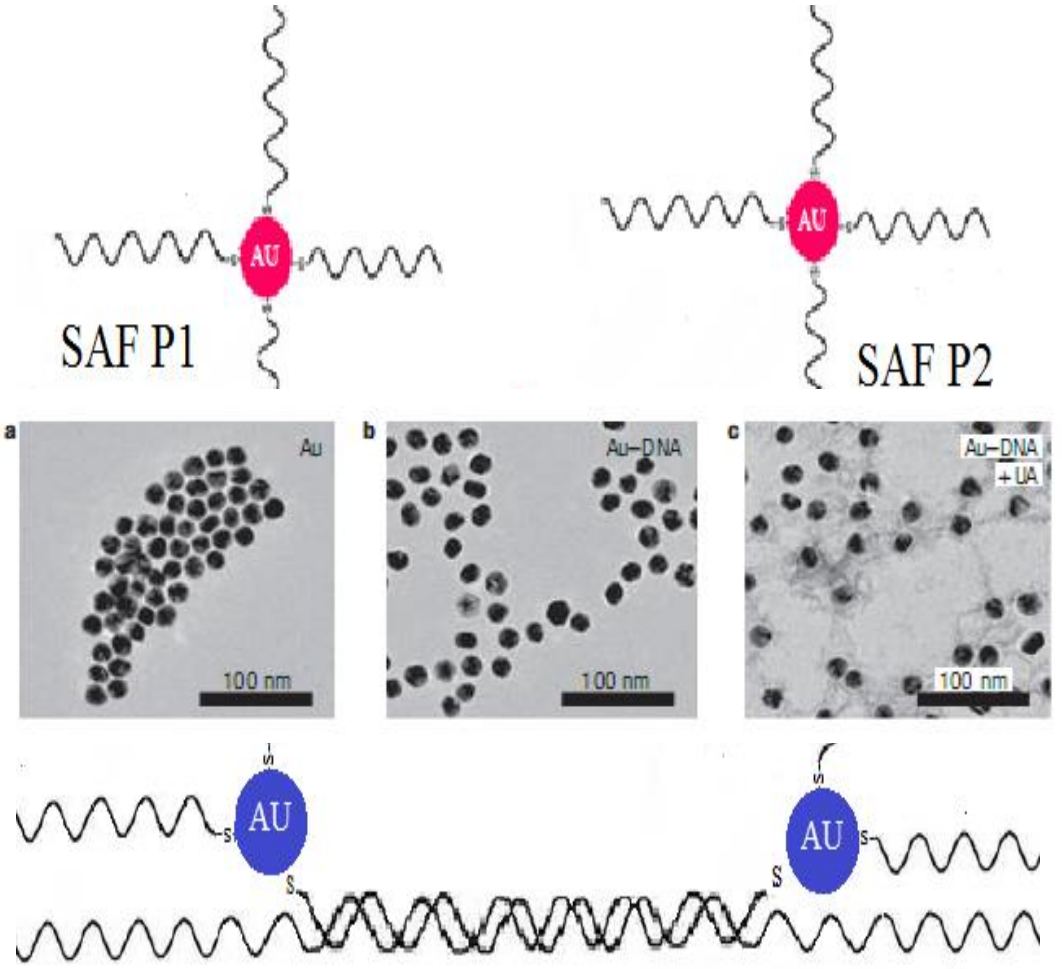
mixing the two DNA–AuNP probes with the target

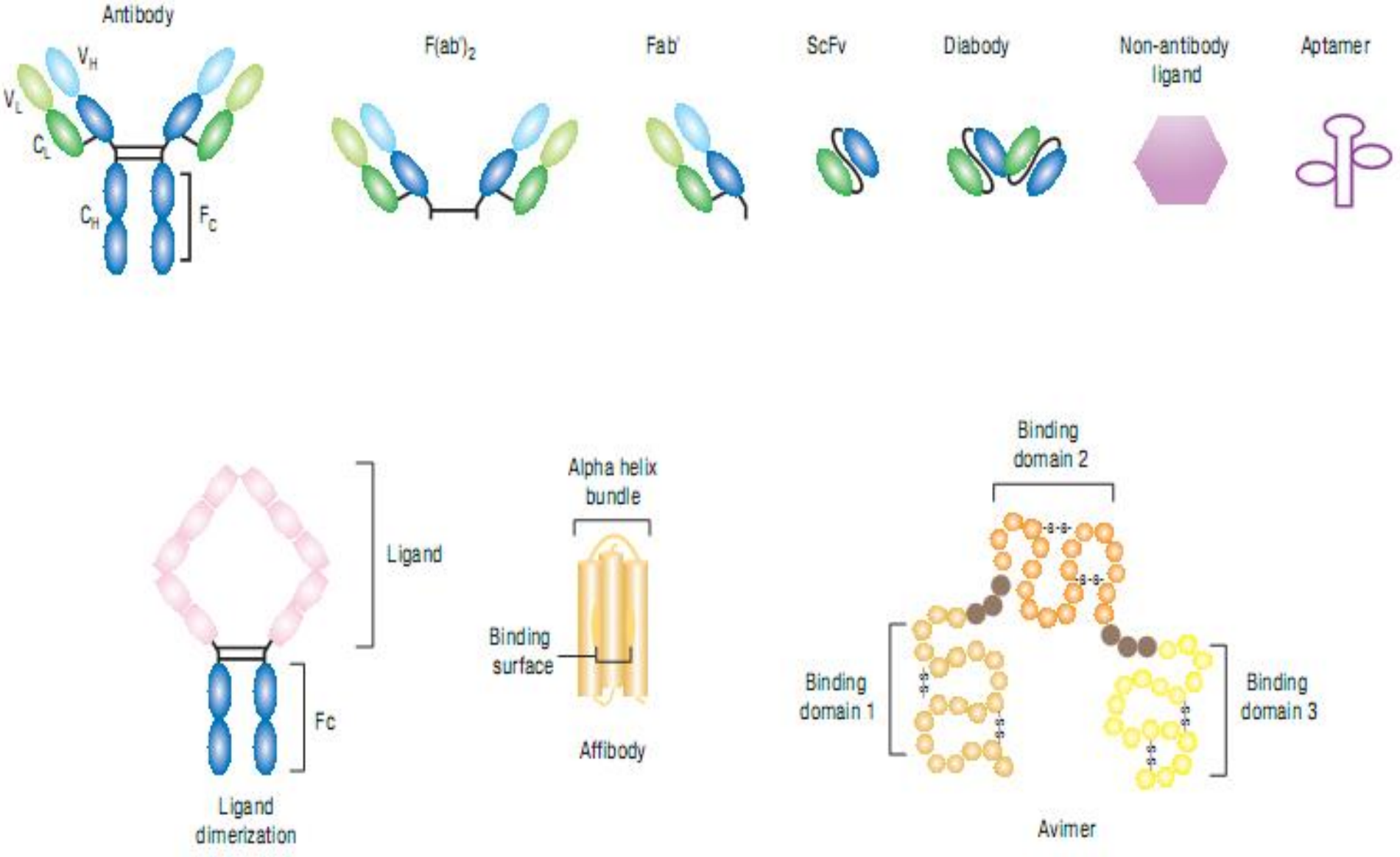
▼

resulted in formation of a polymeric network of DNA–AuNPs

▼

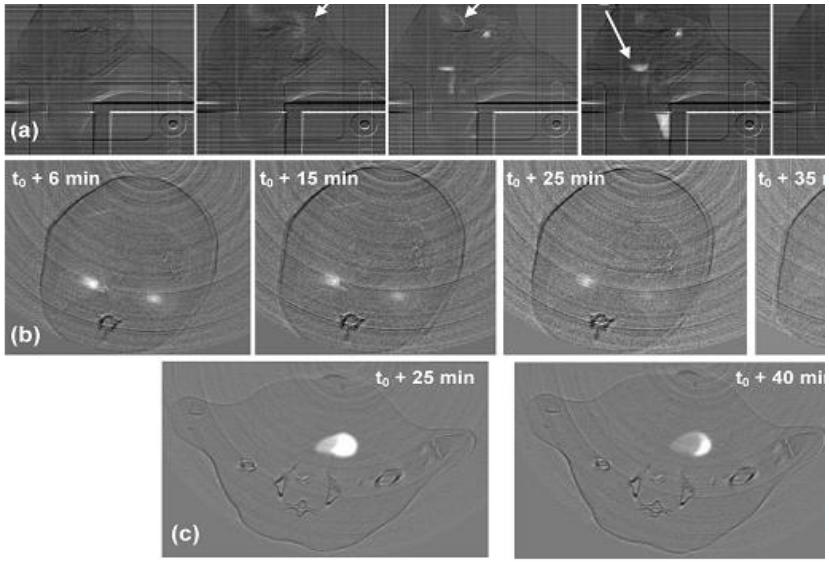
red to purple




Antibody
V_H
V_L
C_L
C_H
F_C
$F(ab')_2$
Fab'
ScFv
Diabody
Non-antibody ligand
Aptamer
Ligand
Fc
Ligand dimerization
Alpha helix bundle
Binding surface
Affibody
Binding domain 2
Binding domain 1
Binding domain 3
Avimer

QD Localization of a Tumor

A. It is possible to overlap X-ray images with infrared images to localize a tumor. The X-ray images give the images an anatomical context, while the infrared images detect the QD's emission, which correlates to the tumor location (see B.)



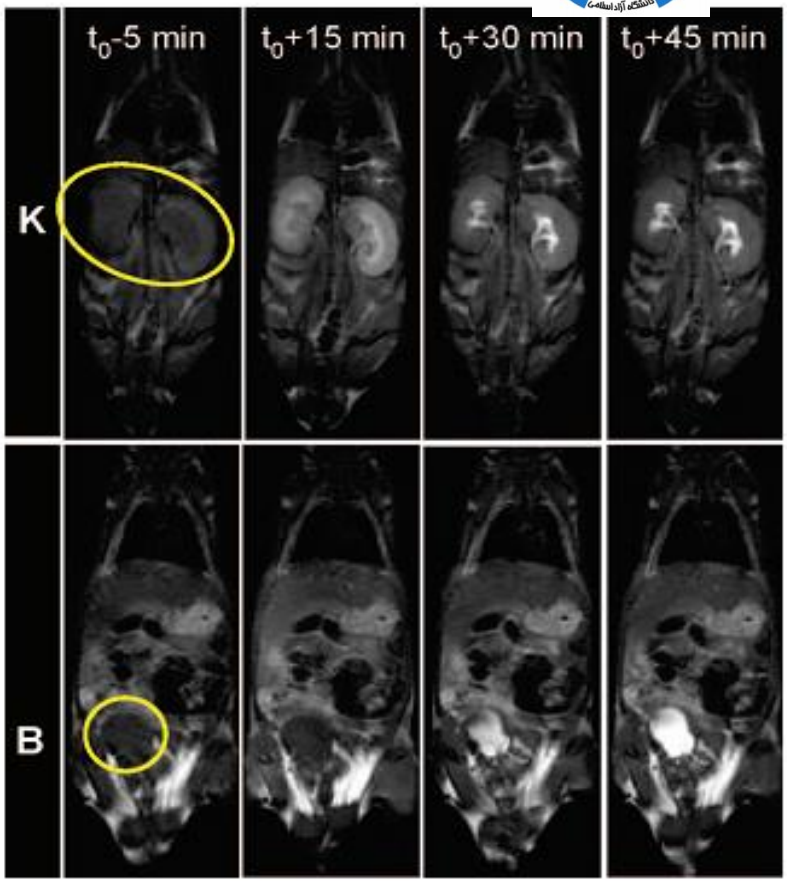
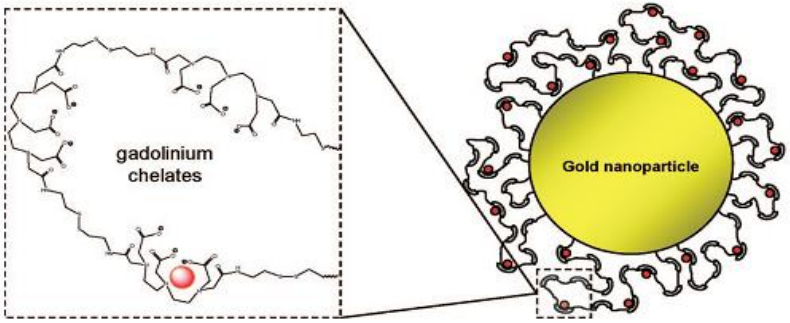
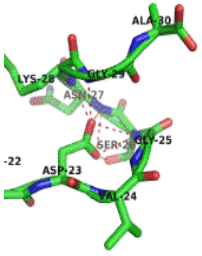


Figure 4. (a) Planar X-ray images in transmission mode of a rat before (t_0 − 2 min) and after injection of Au@DTDT B for bladder and WC for the tube collecting the urine). SPECT images of transverse slices recorded at various times to a rat including (b) kidneys and



Source: www.internetchemistry.com



cal structure of Aβ-protein

Source: wwwthefutureofthings.com

D. Gold nanoparticles can be functionalized to specifically attach to aggregates of this protein (amyloidosis)

Colorimetric contrast of nanoprobes

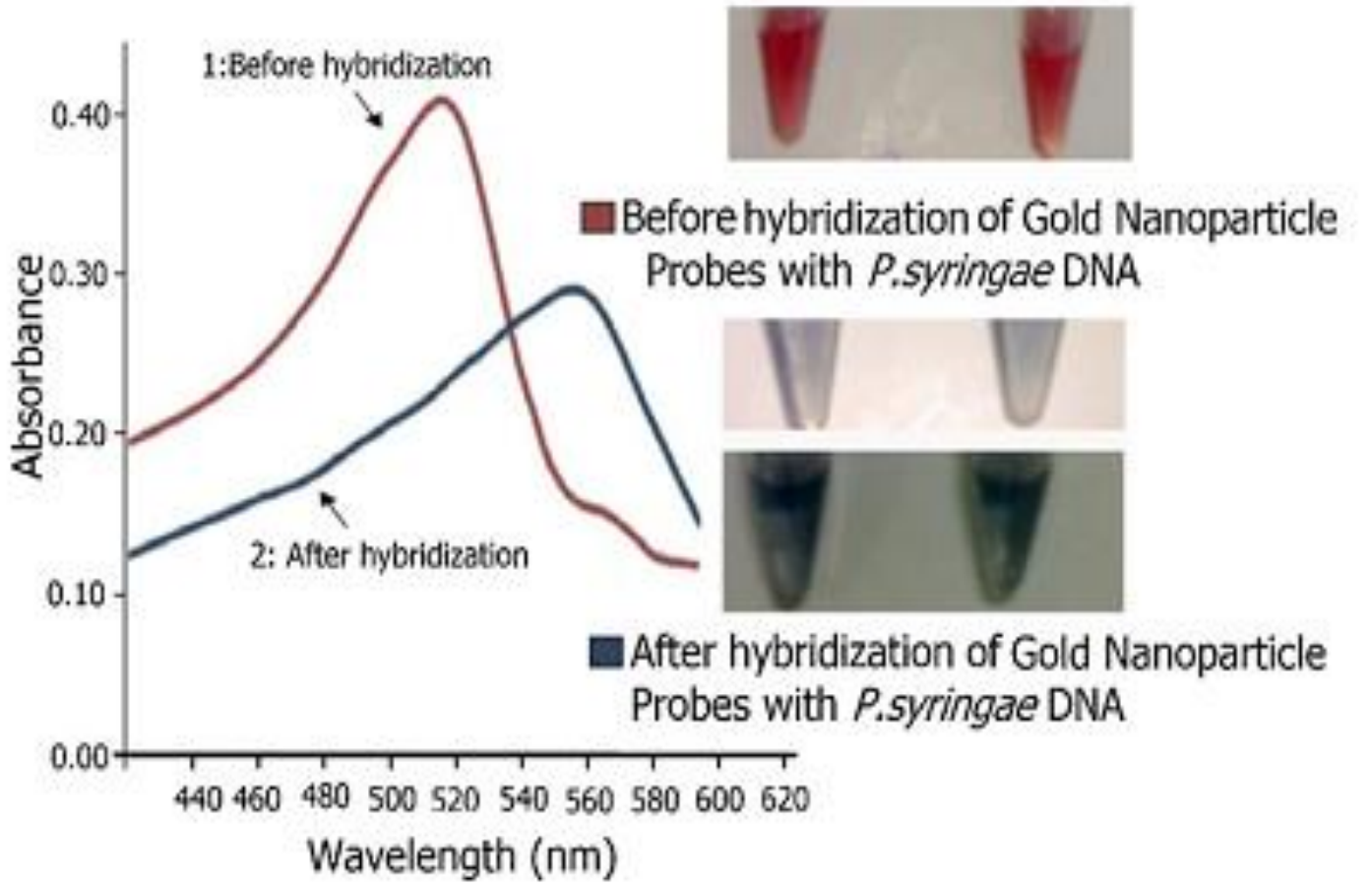


Fig. 2. The average absorbance spectrum obtained before (red) and after (blue) hybridization of Gold NP-bound probes with DNA extracted from 26 pathovars of *P. syringae*. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

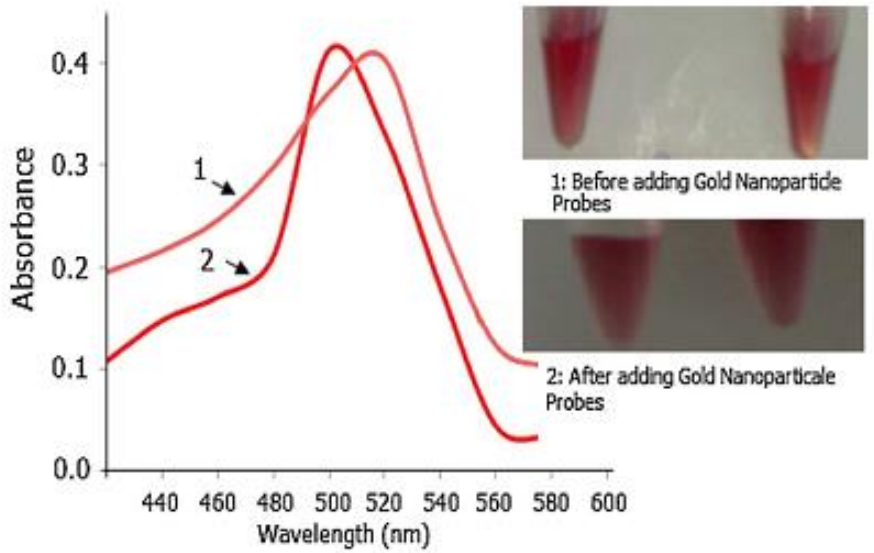


Fig. 3. The average absorbance spectrum for negative control samples, before (1) and after (2) adding Gold-NP bound probes.

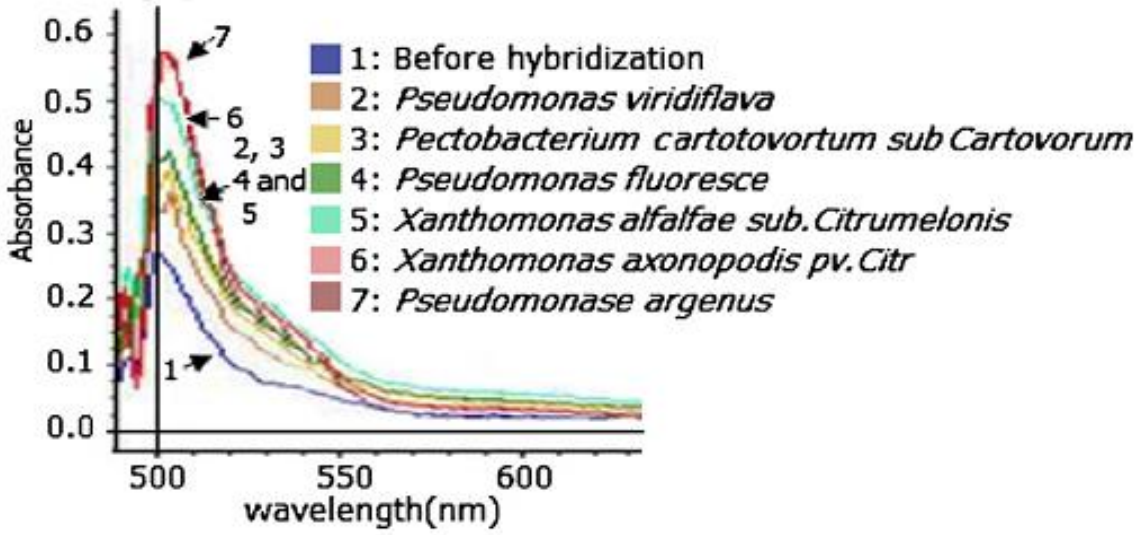


Fig. 4. The absorbance spectrum obtained before (1) and after (2–7) adding Gold-NP bound probes to DNA isolated from bacterial species selected as negative control including *P. viridiflava* (2), *P. cartotovortum* sub *cartovorum* (3), *P. fluoresce* (4), *X. alfalfae* subsp. *Citrumelonis* (5), *X. axonopodis pv. Citr* (6) and *P. Argenus* (7). Adding Gold-NP bound probes to DNA of negative control bacteria did not lead to any alteration in absorbance spectrum for bacterial DNAs.

Determining specificity of hybridization of Gold NP-bound probes with targ

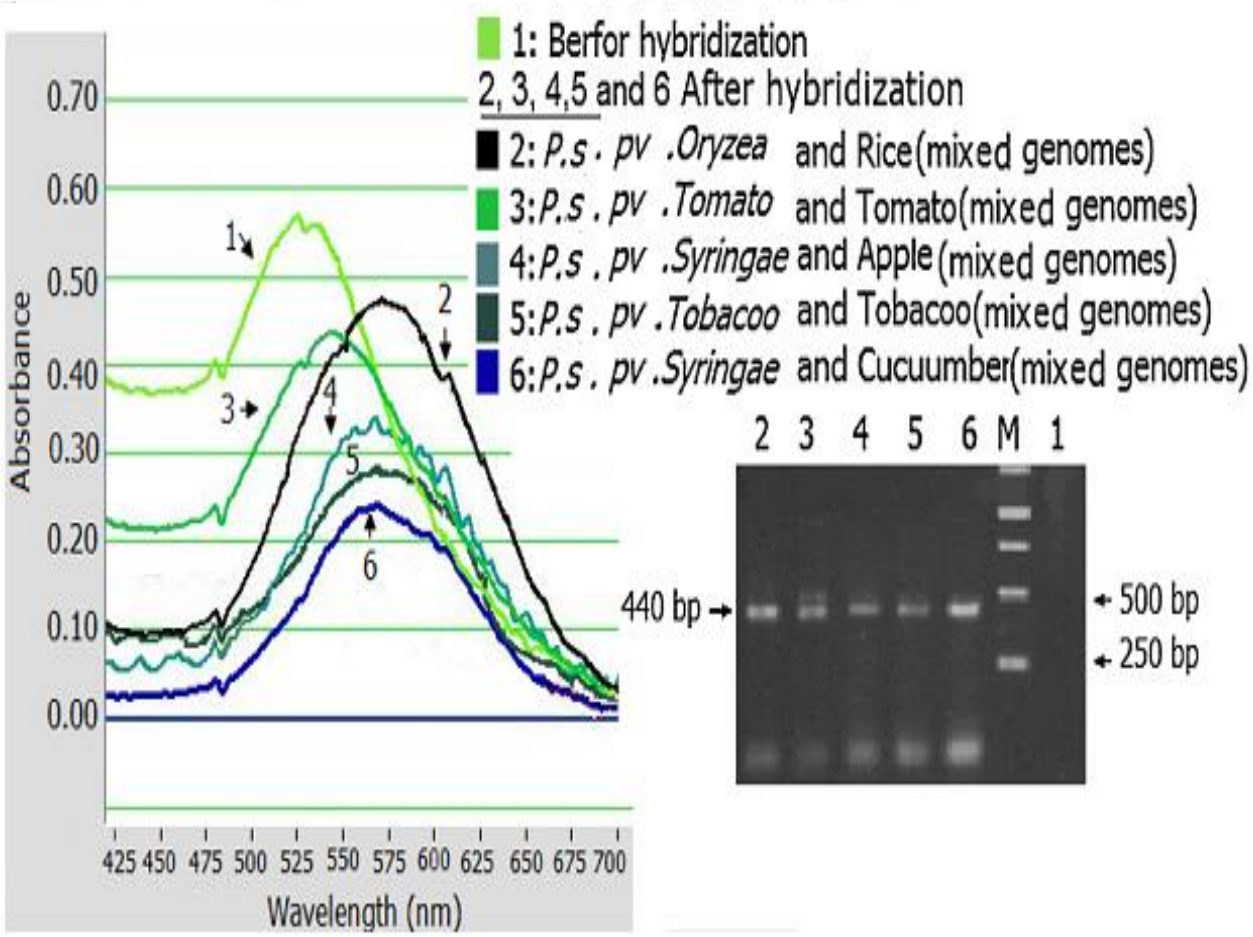


Fig. 5. Gel electr
(2–6) (the right
alteration in abs

Fig. 6. Gel electrophoresis of PCR amplification conducted on DNA extracted from the mixture of plant and bacterial DNA (the right side). Adding Gold-NP bound probes to PCR product resulted in alteration of absorbance spectrum for the mixture of plant DNA and their specific bacteria due to the presence of the *hrcV* gene (numbers 2–6) (the left side). 1 indicates the graph before hybridization of probes.

Determining sensitivity of hybridization of Gold NP-bound probes with targ

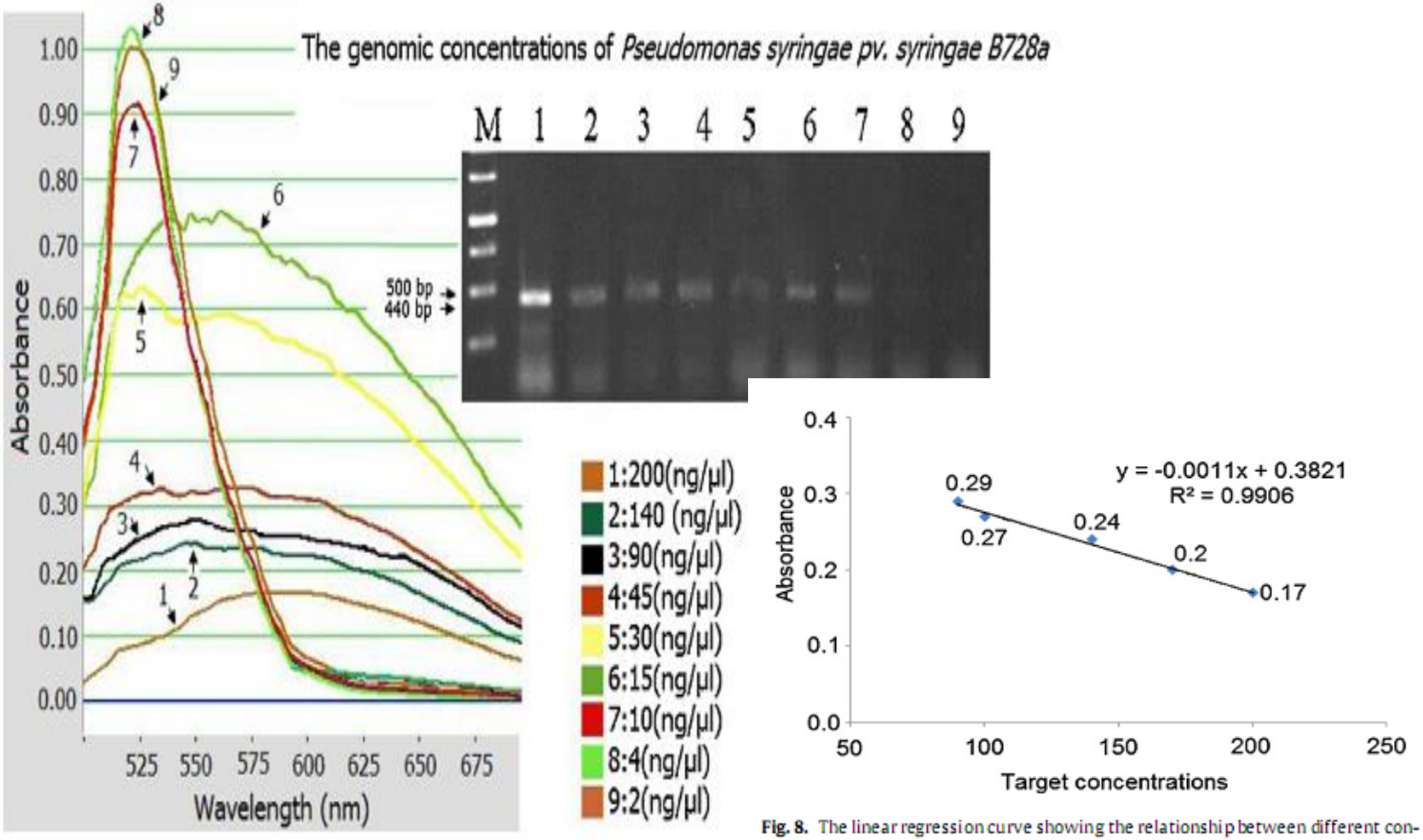


Fig. 8. The linear regression curve showing the relationship between different concentrations of target bacterial DNA and absorbance.

Fig. 7. Determining sensitivity of hybridization of Gold-NP probes with PCR-amplified DNA from *P. syringae pv. Syringae B728a* by testing various concentrations of bacterial genomic DNA ((1) 200 ng/mL, (2) 140 ng/mL, (3) 90 ng/mL, (4) 45 ng/mL, (5) 30 ng/mL, (6) 15 ng/mL, (7) 10 ng/mL, (8) 4 ng/mL and (9) 2 ng/ml).

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Detection of *Pseudomonas syringae* pathovars by thiol-linked DNA–Gold nanoparticle probes

Akbar Vaseghi[a,c], Naser Safaie[b,*], Babak Bakhshinejad[c], Afshin Mohsenifar[d], Majid Sadeghizadeh[c,e,**]

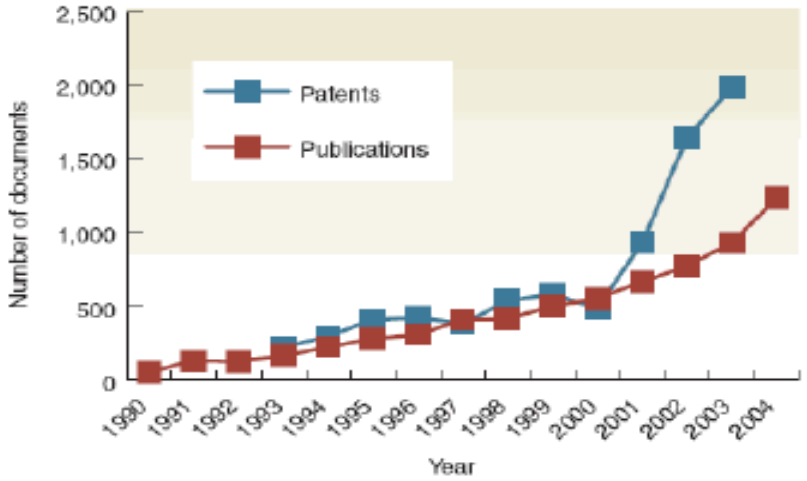
[a] Department of Biotechnology, Faculty of Agriculture, Tarbiat Modares University, Tehran, Iran
[b] Department of Plant Pathology, Faculty of Agriculture, Tarbiat Modares University, Tehran, Iran
[c] Department of Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran
[d] Department of Toxicology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
[e] Department Nano Biotechnology, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran

Transfer of Pathogenicity Proteins for Investigating Vertical and Horizontal Gene Islands in Pseudomonas Species *J. Iran. Chem. Soc., Vol. 9, Suppl. 1, June 2012, pp.*A1- A144(abstract)

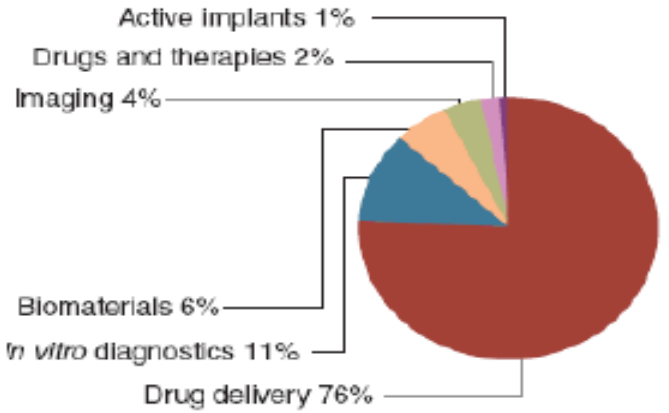
Therapeutic:

Interesting facts about nanomedicine

A. Interest in the area has grown exponentially



B. Drug delivery is the most productive area



C. Drug delivery is the most established technology in the nanomedicine market

Table 1 Commercial efforts in nanomedicine[a]

			Product pipeline		
Healthcare sector	Number of products	Sales ($ billions)	Total	Advanced stages[b]	Companies
Drug delivery	23	5.4	98	9	113
Biomaterials	9	0.07	9	6	32
In vivo imaging	3	0.02	8	2	13
In vitro diagnostics	2	0.78	30	4	35
Active implants	1	0.65	5	1	7
Drugs & therapy	0	0	7	1	7
Total	38	6.8	157	23	207

[a]Sales numbers of nanomedicines are estimates for the year 2004. [b]Drugs where the product is in clinical phase 2/3 or 3 and for all other products where market introduction is expected within two years.

Nature Biotechnology 2006, Vol. 4, pp.1212-1217

Therapeutic:

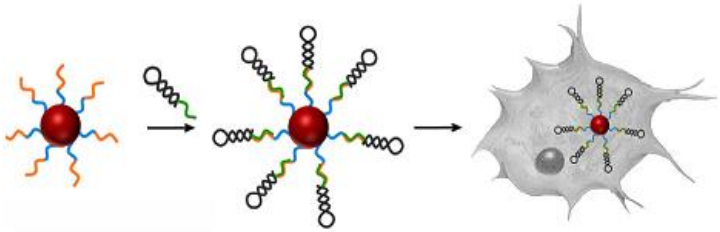
Table 2 Examples of nano-based platforms and their current stage of development for use in cancer therapy

Type of carrier and mean diameter (nm)	Drug entrapped or linked	Current stage of development	Type of cancer (for clinical trials)	References
Polymer–drug conjugates (6–15)	Doxorubicin, Paclitaxel, Camptothecin	12 products under clinical trials	Various tumours	Reviewed in 3, 61
Lipos (85–				
Polyı (50–				
Polyr				
Mice (5–1				
Nanc Gold Nanc				
Dend Imm Imm				
Imm fusion proteins (3–15)				16, 17, 61

Examples of the use of gold nanoparticles in clinical practice

Type of Gold Nanoparticle	Nanoparticle Size (nm)	Role	Disease State	Sponser/Lab
Nanosphere	13	siRNA delivery	Unspecified	Mirkin
Nanorod	10 × 40	Photothermal ablation; CT contrast and thermal imaging	Unspecified	Bhatia
Gold-silica Nanosphere	60/140	Raman Imaging	Colon Cancer	Gambhir
Gold Nanoshell (Aurolase™)	150	Photothermal therapy	Head and Neck cancer	NanoSpectra NCT00848042
Gold Colloidal Nanosphere (Aurimune™)	27	Stimulate immune response to tumor growth	Solid Tumors	NCI NCT00436410

Various applications of gold nanoparticles in therapy



sh RNA :

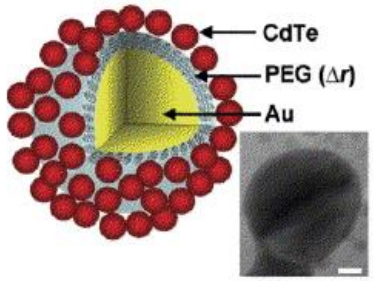
sh RNA -P53 :

shRNA-Mcl-1L :

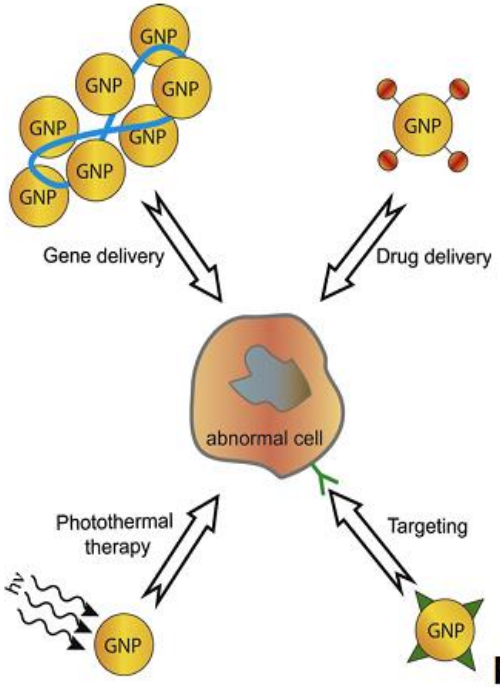
Cargo DNA :

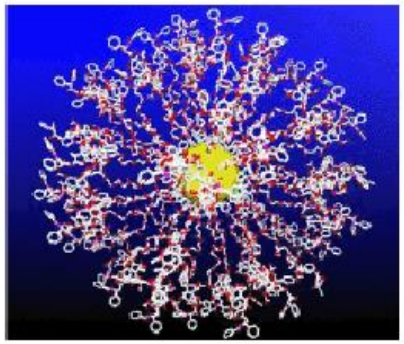
Gold nanoparticle :

mic RNA,cDNA,ncRNA,siRNA, GENOME,

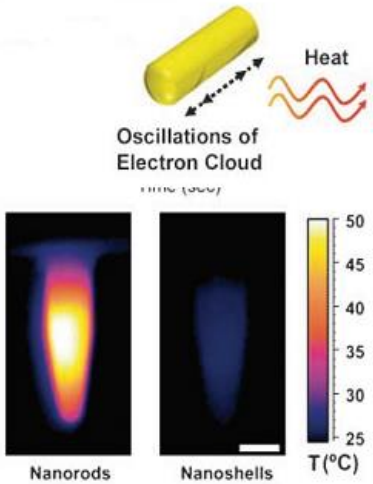


Angew. Chem. Int. Ed. 2005, Vol. 44, 7439 –7442



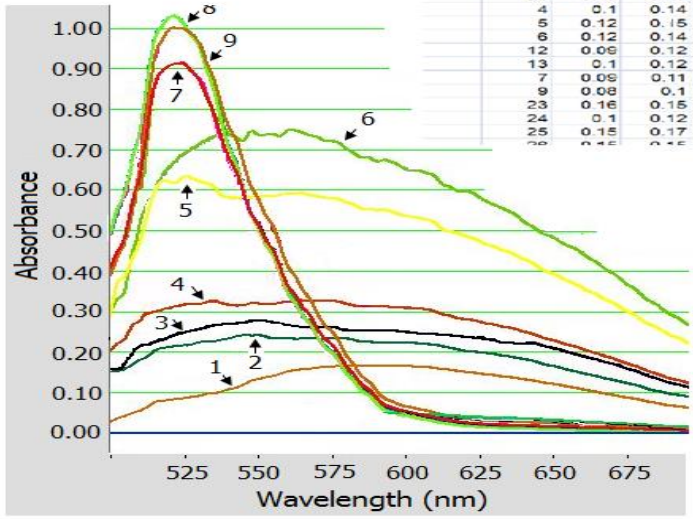


Functionalized Dendrimer **G4** by Gold-Nanoparticles



Nanorods **Nanoshells**

PEPTIDE
(Detection and Treatment)
ANTIBODY
APTAMER



3	0.1	0.13	0.13	0.14	0.18	0.19
15	0.15	0.18	0.18	0.2	0.24	0.26
16	0.15	0.17	0.19	0.21	0.25	0.25
17	0.16	0.17	0.19	0.2	0.23	0.2
18	0.17	0.18	0.19	0.21	0.24	0.25
19	0.15	0.17	0.18	0.2	0.27	0.27
21	0.15	0.18	0.19	0.22	0.25	0.25
4	0.1	0.14	0.17	0.2	0.28	0.3
5	0.12	0.15	0.18	0.23	0.32	0.32
6	0.12	0.14	0.18	0.22	0.27	0.34
12	0.09	0.12	0.16	0.2	0.24	0.31
13	0.1	0.12	0.17	0.23	0.29	0.35
7	0.09	0.11	0.14	0.17	0.17	0.24
9	0.08	0.1	0.12	0.17	0.18	0.25
23	0.16	0.15	0.19	0.2	0.23	0.18
24	0.1	0.12	0.15	0.17	0.2	0.19
25	0.15	0.17	0.17	0.2	0.24	0.21

Discussion and Conclusion

- Future research will need to determine the optimal gold nanoparticles for each potential human application, and inevitably, tradeoffs will have to be made regarding some of their diagnostic and therapeutic properties vis-a-vis their associated toxicity profile. Overall, gold nanoparticles are ideally placed to make the transition from the laboratory benchtop to the clinical bedside in the very near future.

Thank you every body for your kind attention

Young Researcher Club, Science and Researcher Branch, Islamic Azad University, Ardabil, Iran

Prof .Majide Sadeghizade

PhD in Molecular Biology, France, 1995–1997. he is currently employed as full professor in Genetics and Nano-biotechnology and chairman of Genetics Department, Tarbiat Modares University, Tehran, Iran. His fields of interest are Nano-biosensors, Drug and Gene delivery systems, design of Nano-diagnostic systems for detection microorganisms.