Nanomaterials for dental applications:

From academic innovation to commercialisation

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Department of Chemistry, University of Otago

University Club • Mercure Leisure Lodge • 27 July 2018

What are **nano**materials?

What is nanoscience?

The science of small things that are only ***nanometres*** in size.

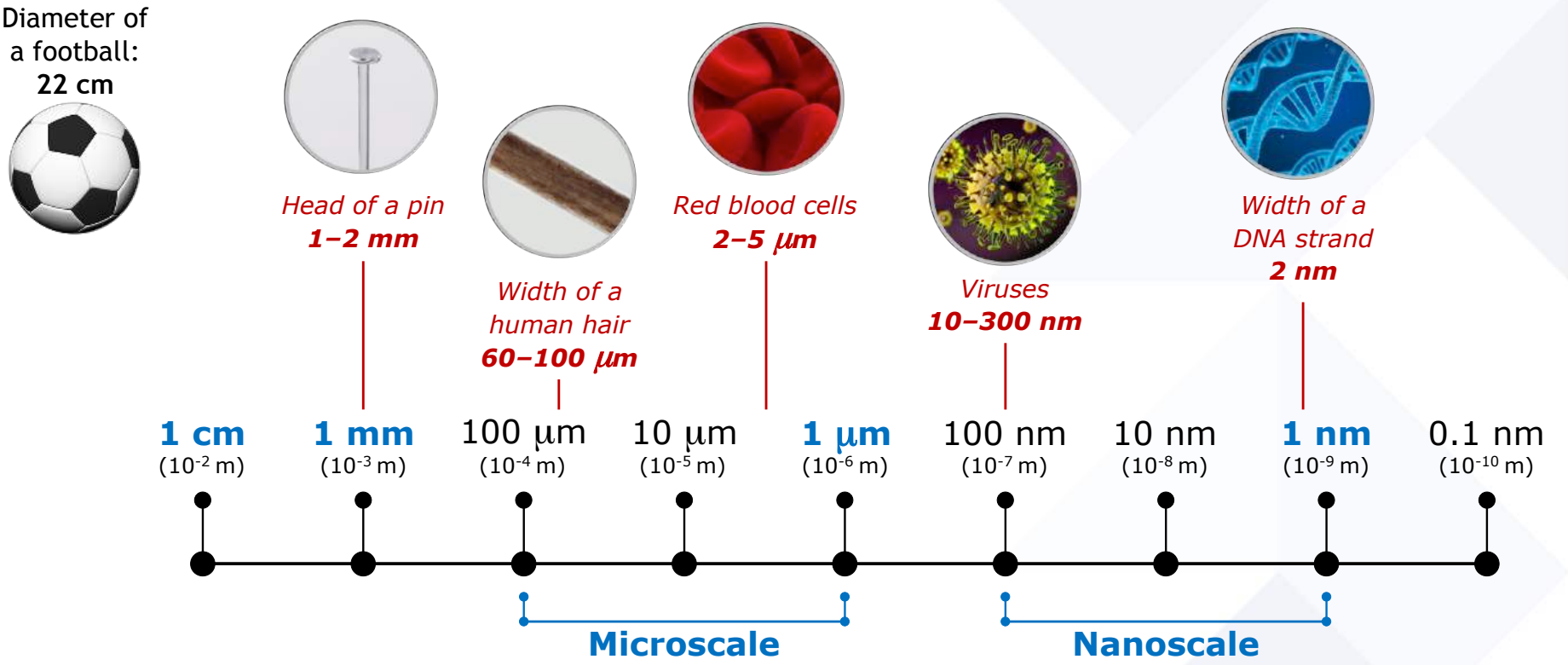
What is nanotechnology?

Building and using materials, devices and machines at the ***nanometre*** scale, making use of unique properties that occur for structures at those small dimensions.

What are nanomaterials?

Materials with at least 1 dimension on the ***nanometre*** size scale.

Just how small is a nanometre?



Why is small good?

Why is small good?

Small materials are good for many reasons:

- Faster
- Lighter
- Can get into small spaces
- Cheaper
- More energy efficient
- **Different properties for very small structures**

This last property makes small materials not only good, but extremely interesting…

Properties of materials on the nanoscale

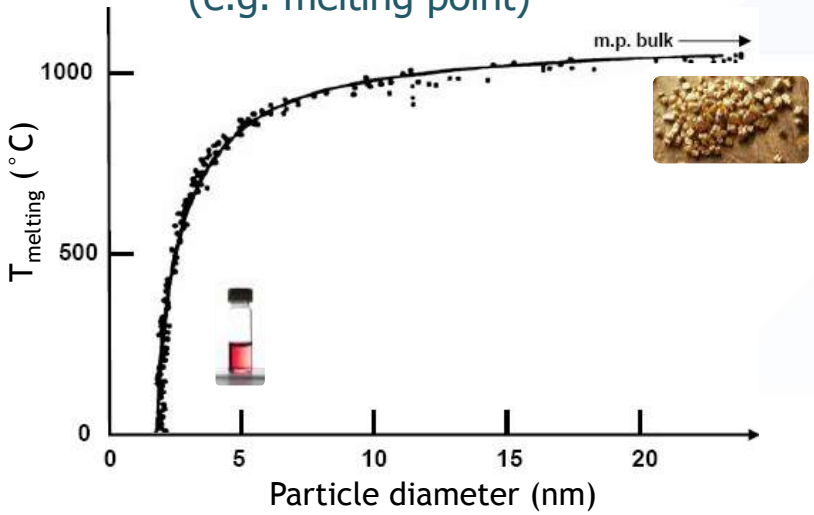
Many of the properties of materials change on the nanoscale & new phenomena emerge!

Optical properties
(e.g. colour)

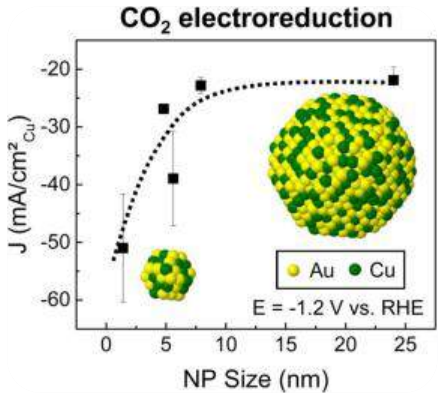
Bulk gold

Nanogold

Physical properties
(e.g. melting point)

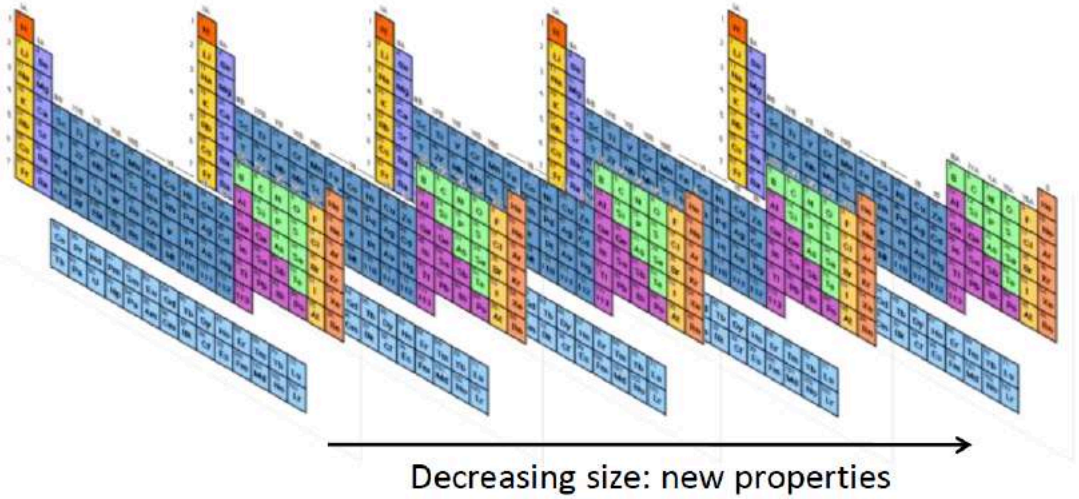


Chemical properties
(e.g. reactivity)



Properties of materials on the nanoscale

Changes of materials properties on the nanoscale gives us a "3rd dimension" to the periodic table.



Advent of new techniques for visualising and manipulating materials on the nanoscale allows for deeper understanding and careful control over the properties of the resulting materials.

What does this have to do with dentistry?

Colloidal-based approaches for the development of functional nanoscale materials

Exploratory

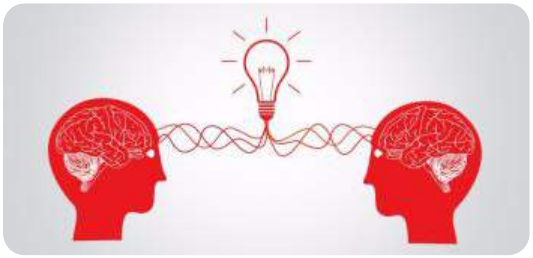
Perform experiments to gain new knowledge & understanding

New Materials

Use knowledge gained from exploratory experiments to make new nanomaterials aimed to solve problems

- Treat/prevent dental diseases
- Antibacterial bone scaffolds to prevent infection
- Improved MRI contrast agents for earlier diagnosis
- Prepare dispersible heterogeneous catalysts
- Improve gas separation/storage using nanoscale porous materials
- Provide surface attachment sites for magnetically-interesting molecules

Meeting of the minds:
when nanoscientist meets dentist



Dr. Don Schwass
Prosthodontist
Faculty of Dentistry
University of Otago

Motivation:

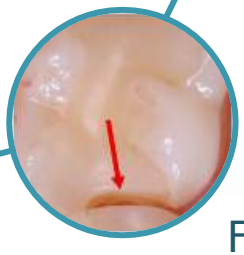
To develop new prevention/treatment strategies for common dental diseases…

through the use of innovative nanoscience & nanomaterials

Dental caries

Bacterial processes lead to demineralisation of hard dental tissues; one of the most common diseases worldwide.

Conventional treatment strategy:
"Drill & Fill"



Reactivation of decay

Failed/chipped restorations

(2-10 year life span for composite fillings)

Peri-implantitis & Periodontitis

Inflammatory disease (gum disease) caused by bacterial infection of supporting tissue around teeth and/or implants

Affects 1 in 3 NZ adults

Conventional treatment strategy:
Scaling and Root Planing (SRP)

Physical disruption of biofilms; chemotherapy with disinfectants and antibiotics

Only capable of slowing the disease process, at best

Historical use of silver in dentistry

Dental amalgam

- mixture of mercury silver, tin and copper

Silver compounds

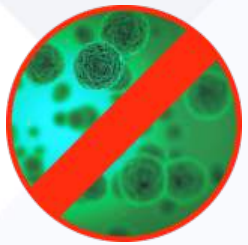
- e.g. silver nitrate, silver fluoride, silver diammine fluoride

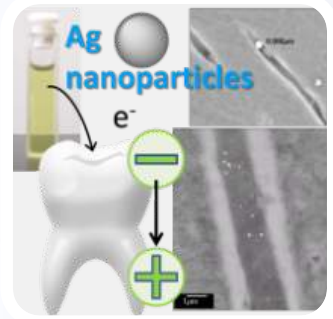
Antimicrobial properties, but…

- high silver content/concentration required (expensive)
- limited penetration into tooth structure
- discolouration/staining of tooth structure

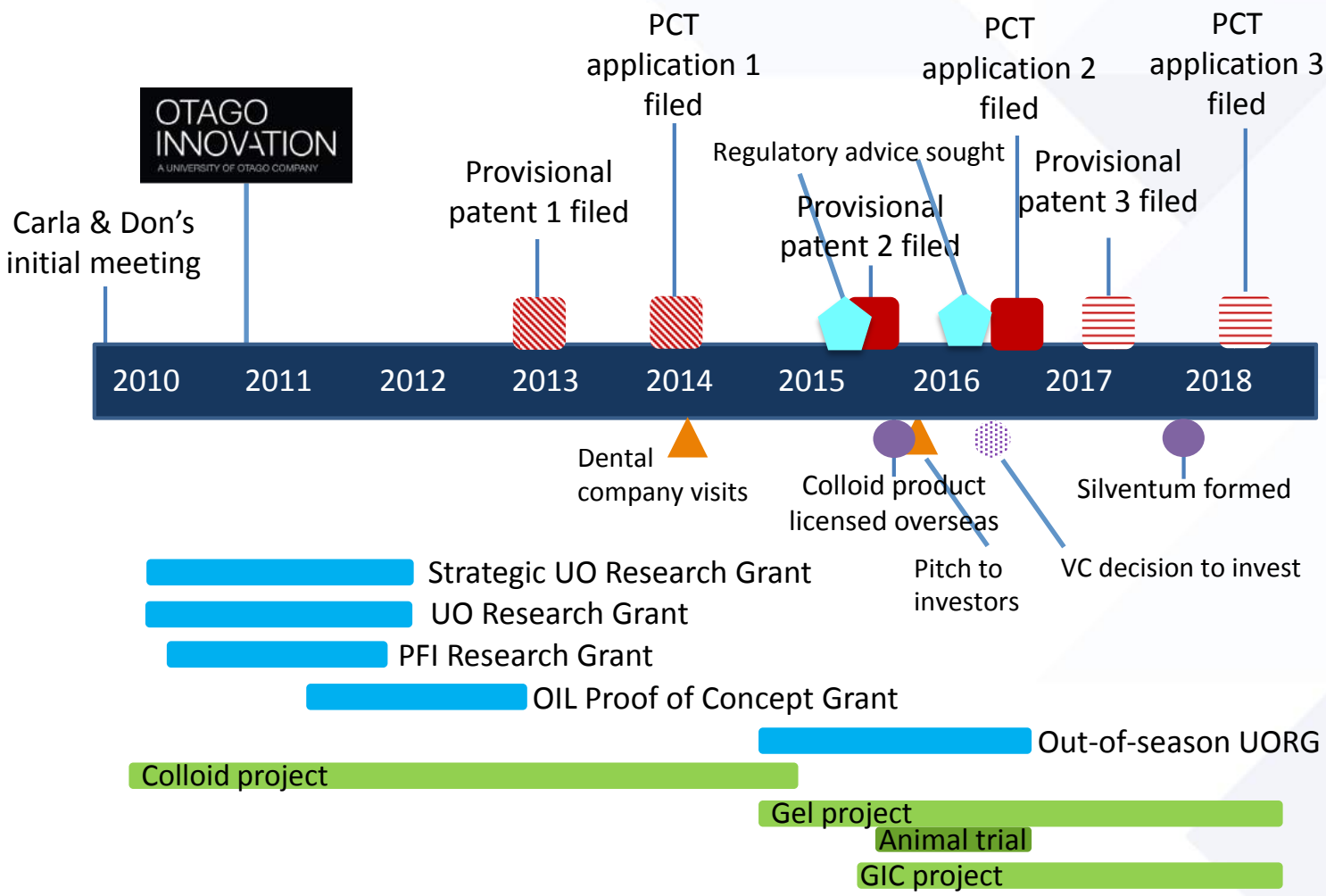
From MACRO to nano:
The unique properties of silver nanoparticles

- Significantly enhanced antimicrobial activity
- High surface area; easily functionalisable surface; targeted delivery to site/source of disease
- Controllable optical properties; can be “tooth coloured”





Timeline toward commercialisation



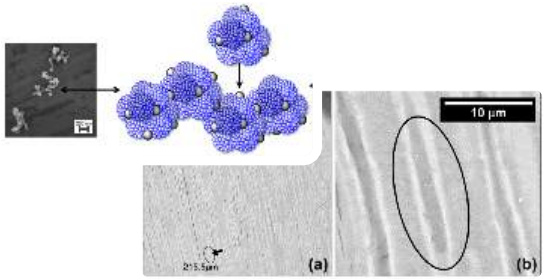
A series of silver NP technologies

1

Colloidal product:

Licensed to a global dental manufacturing company, Aug 2015

Potential for clinical trial in NZ



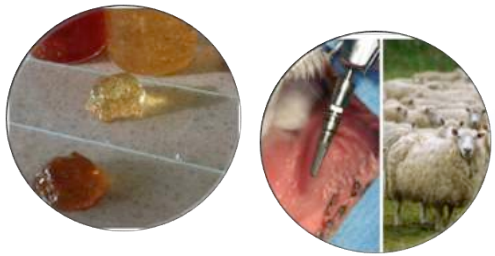
Meledandri C.J, Schwass D.R.
PCT/NZ2014/000006, 24/01/2014
Notice of allowance by USPTO: 27/06/2018

2

Antimicrobial, mucoadhesive hydrogel:

Animal trials completed 2016

Negotiations underway with industry partner



Cotton G.C, Schwass D.R, Meledandri C.J.
PCT/NZ2016/050162, 04/10/2016.

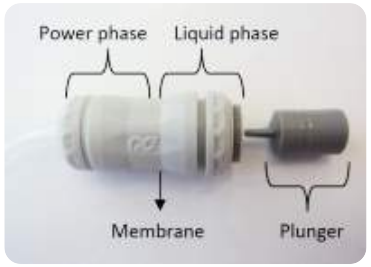
3

Antimicrobial dental filling materials:

Spin-out company:
Silventum Limited
Incorporated Sept 2017

Cotton G.C, Schwass D.R, Meledandri C.J.
PCT/NZ2018/050073, 24/05/2018.

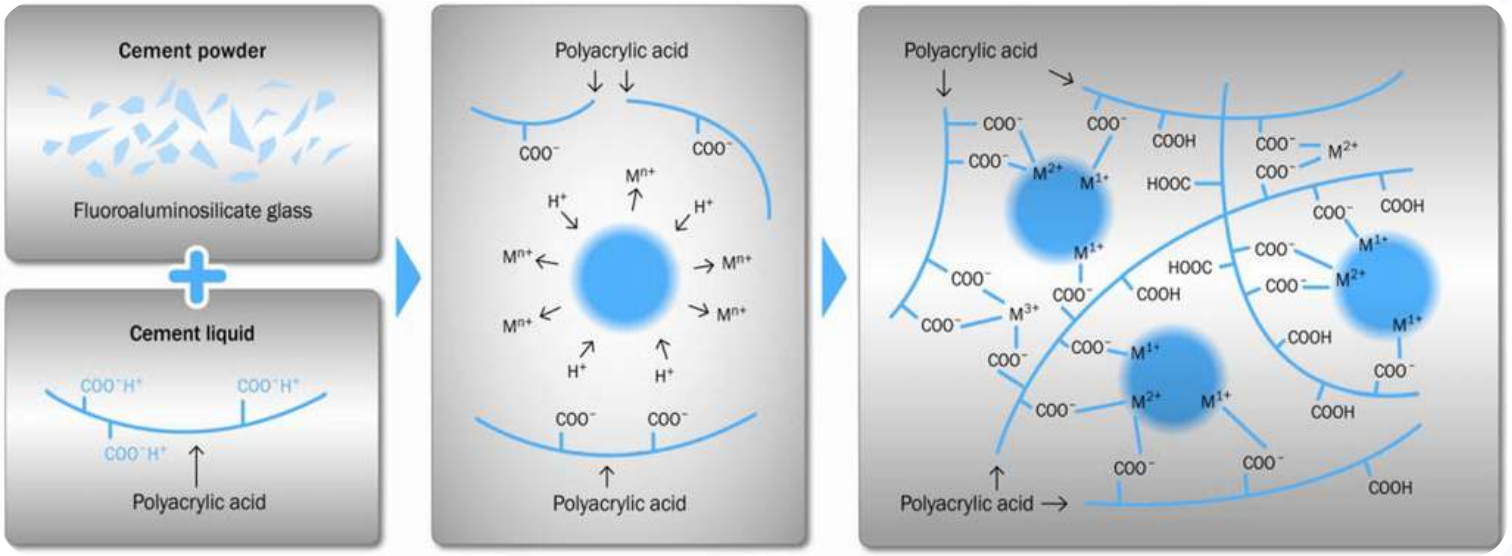
Glass ionomer cements (GICs)



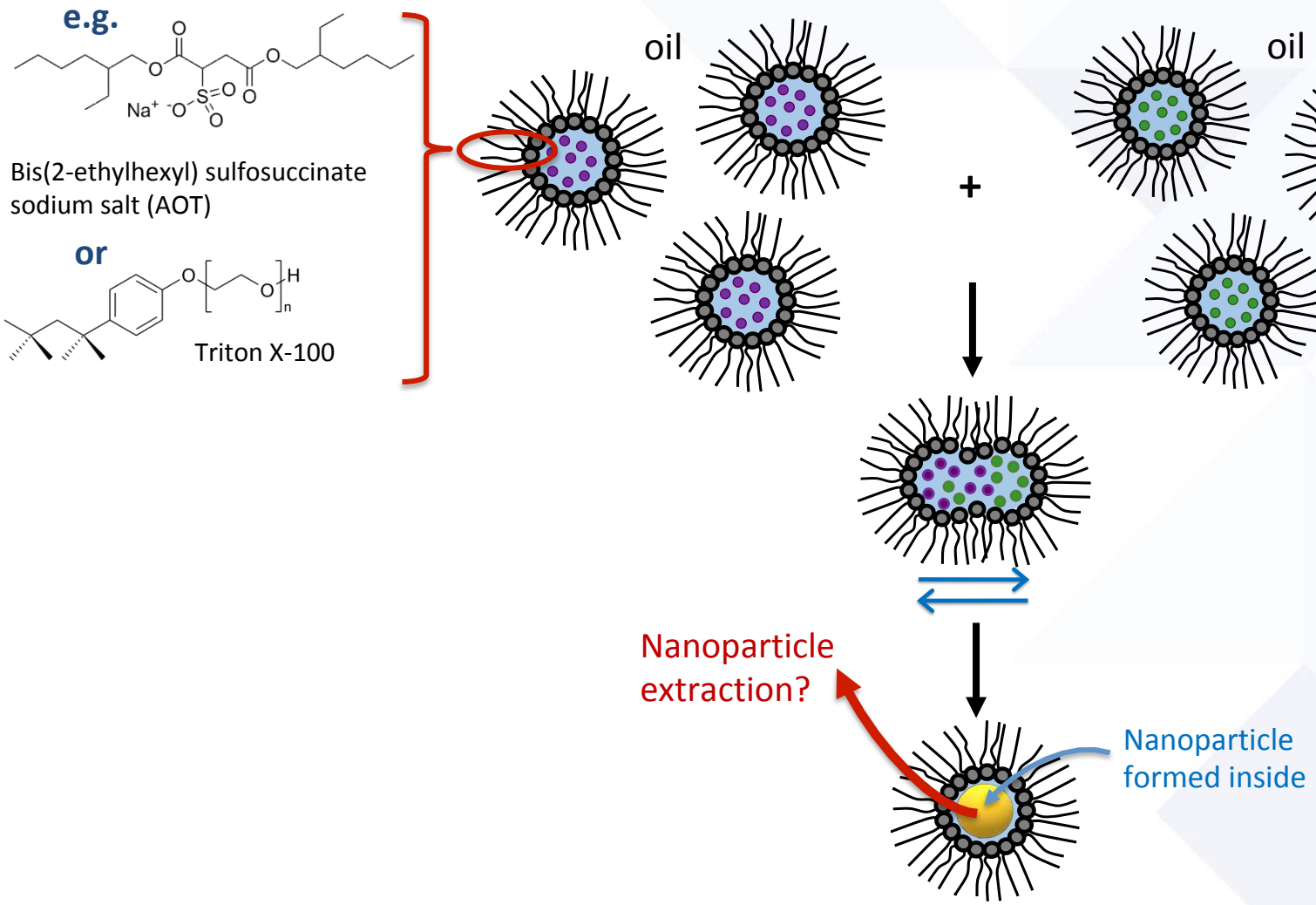
Fuji IX
(GC Corporation; Tokyo, Japan)

–COO^- surface functionality on silver nanoparticles desired

GIC Chemistry



Preparation of functionalised silver nanoparticles



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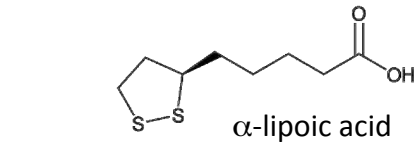
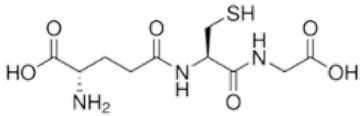
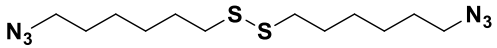


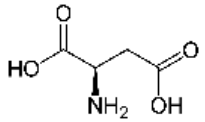
α-lipoic acid



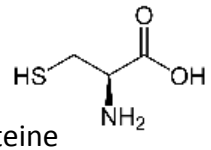
L-glutathione



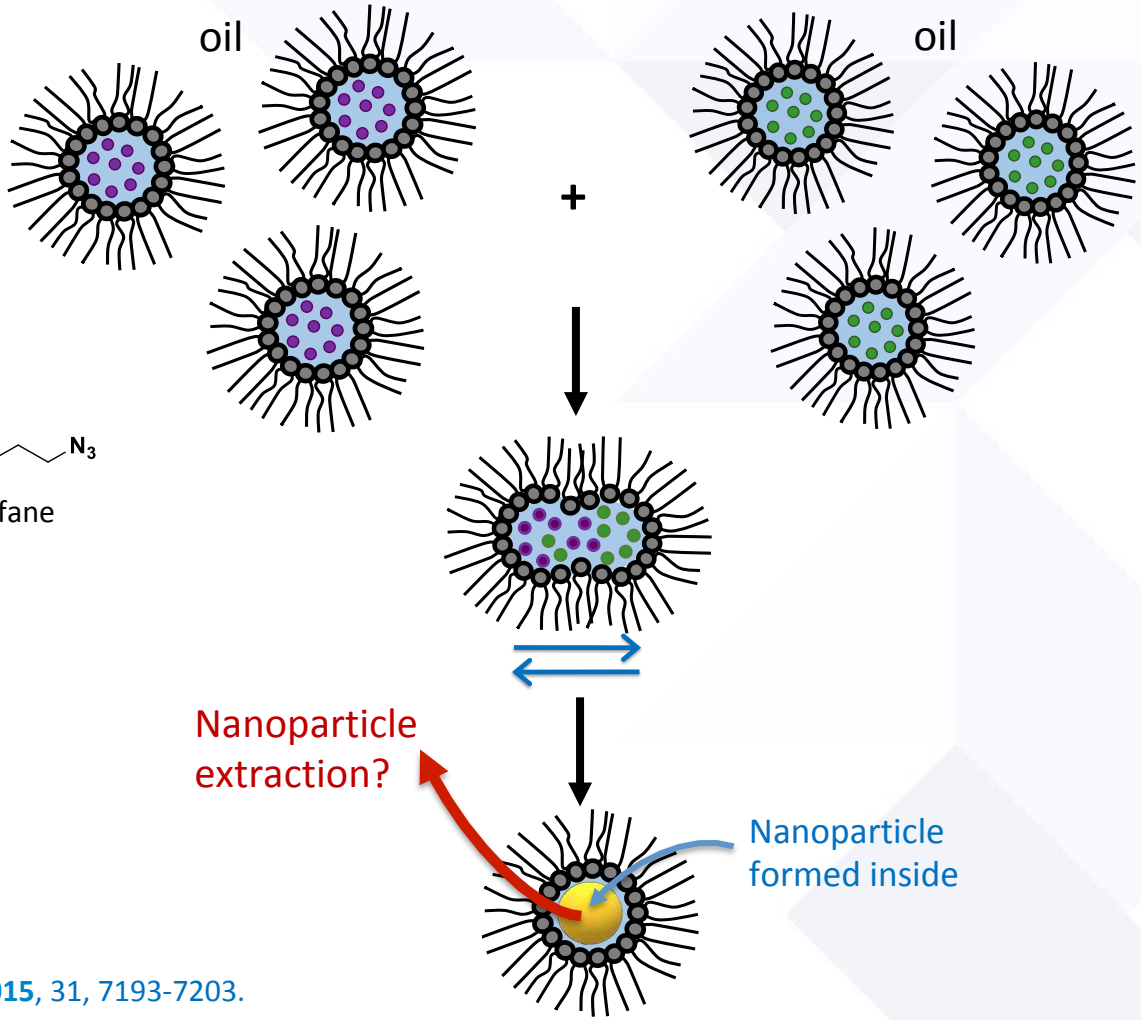
1,2-bis (6-azidohexyl) disulfane



L-aspartic acid



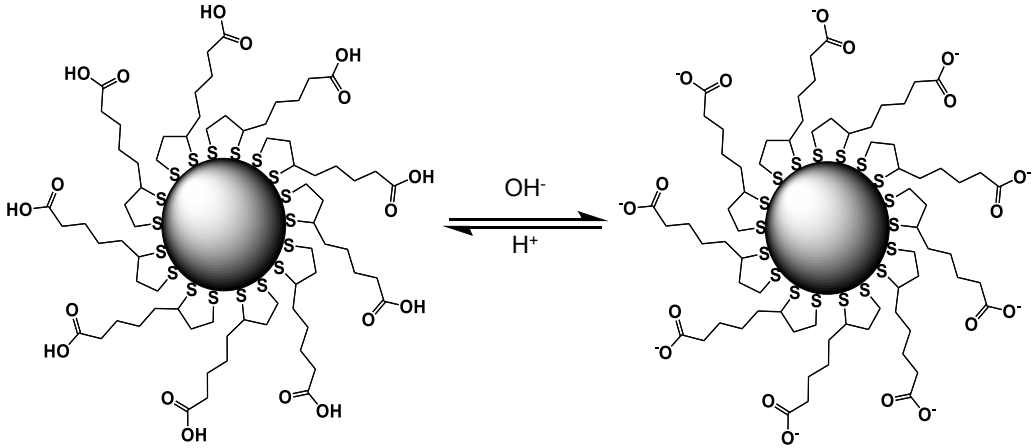
L-cysteine

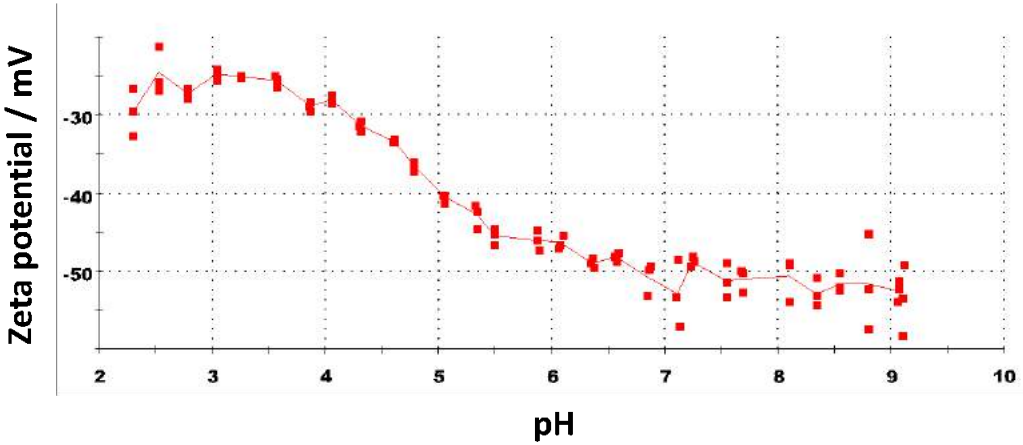


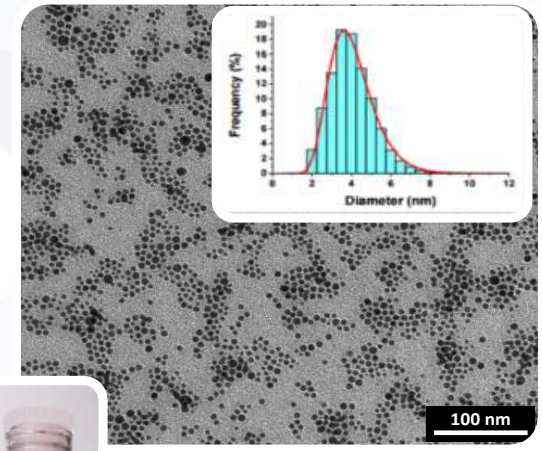
Dumas, C.; Meledandri, C. J. *Langmuir*, **2015**, 31, 7193-7203.

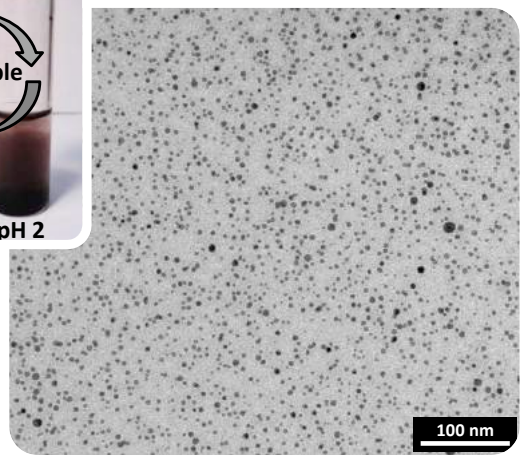
Preparation of functionalised silver nanoparticles

–COO^- surface functionality on silver NPs desired



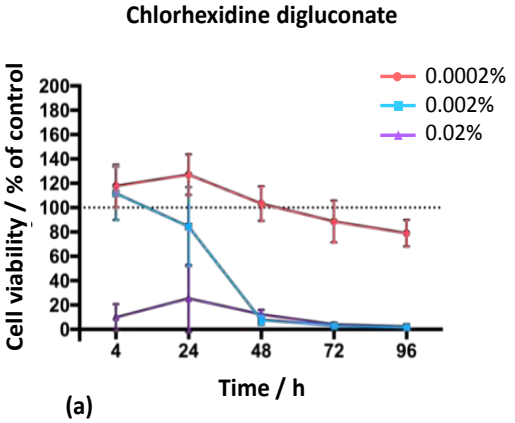


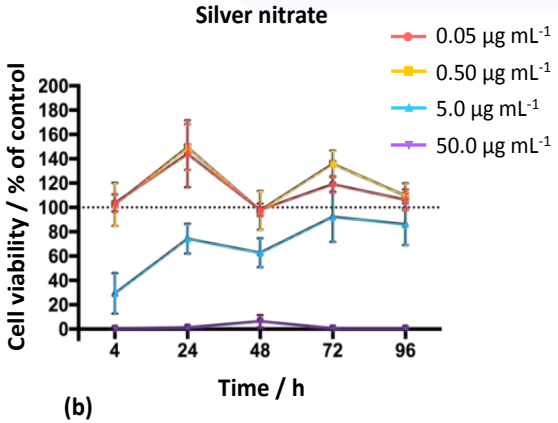


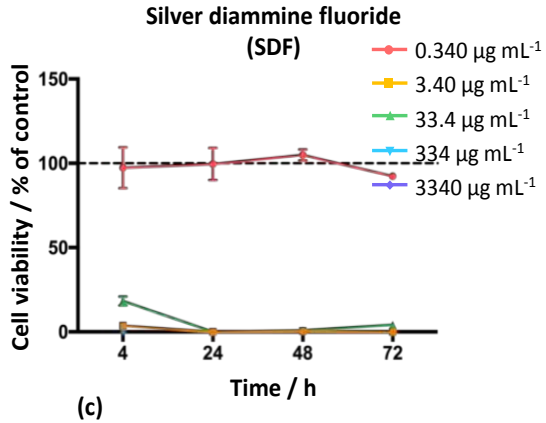


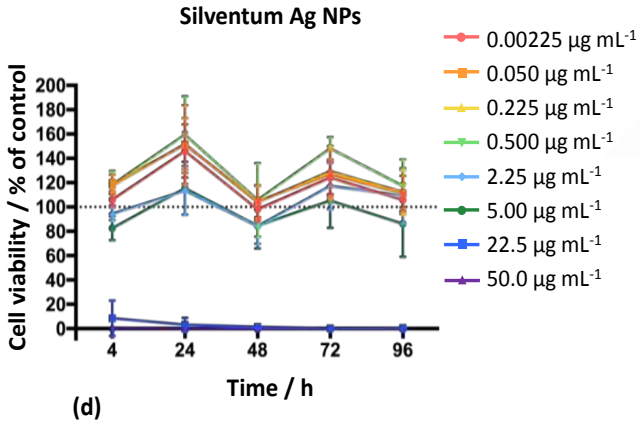
Toxicity studies

The toxicity of thioctic acid-Ag NPs was tested against human gingival fibroblast (HGF) cells









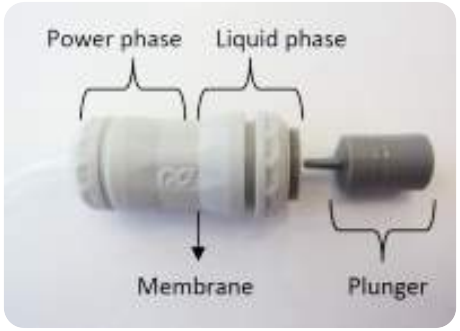
Thioctic acid-Ag NPs are **not** cytotoxic to HGF cells at [Ag] ≤ 5.0 µg mL^{-1} (IC_{50} = 10.4 µg mL^{-1}).

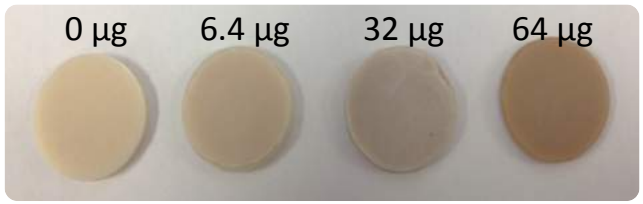
At the same [Ag], both silver nitrate and SDF **are** cytotoxic.

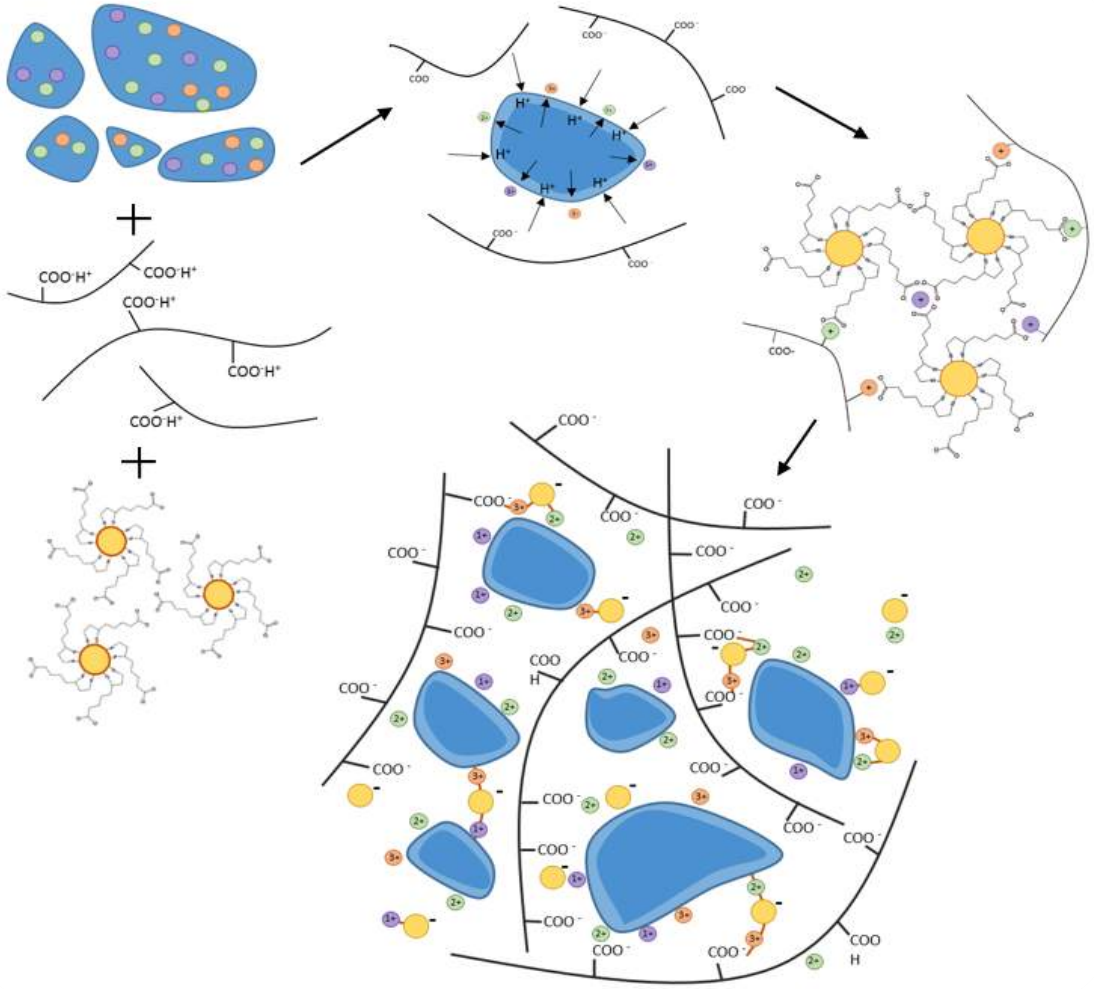
The accepted clinical dose of SDF is 334,000 µg mL^{-1}.

Chlorhexidine digluconate, commonly present as an antibacterial agent in commercial mouthwash products at concentrations ranging from 0.02% to 0.3%, demonstrated cytotoxic effects at concentrations ≥ 0.002%.

Ag NP-modified GICs

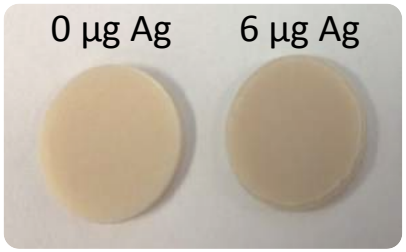






Silver-modified GICs

silventum



6 µg of silver
(0.000006 g)

Light colour

"The light grey colour of Riva Silver requires minimal masking when used under aesthetic restorations."

Riva Silver contains a minimum of
220,000 µg of silver
(0.22 g)

3MESPE

Ketac Silver contains a minimum of
200,000 µg of silver
(0.20 g)

Luting material, dentine replacement, adhesive, restorative material

Antimicrobial activity of GICs: planktonic cells

Broth dilution method

S. gordonii (+)

S. mitis (+)

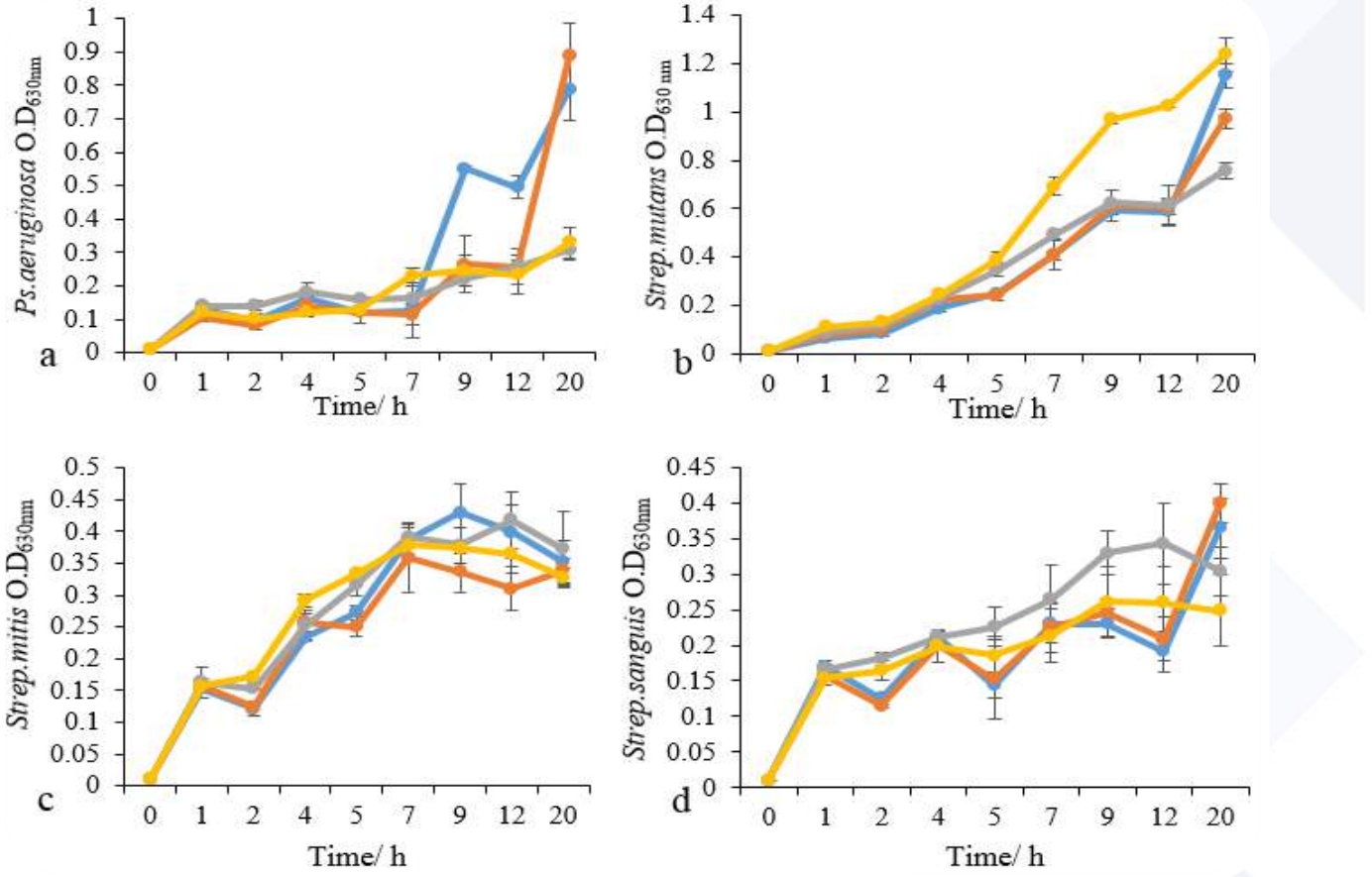
S. mutan (+)

S. oxford (+)

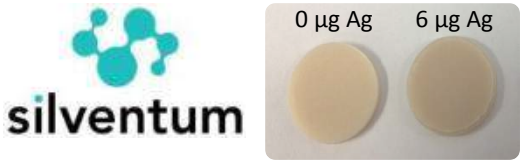
E. faecalis (+)

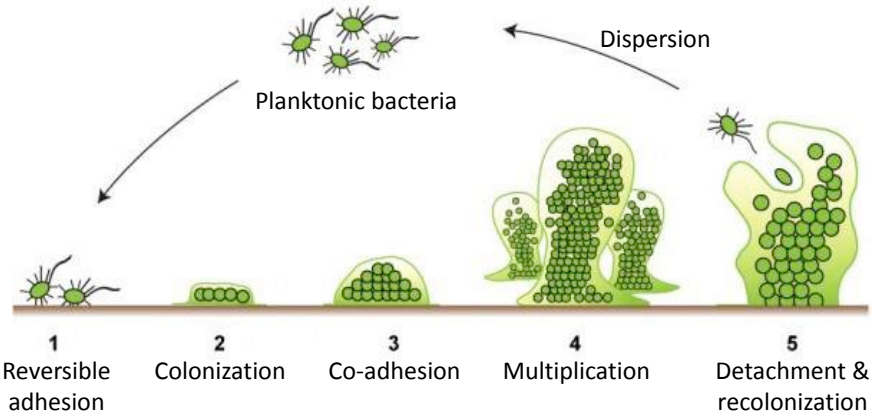
P. aeruginosa (-)

E. coli (-)



Antimicrobial activity of GICs: biofilm prevention



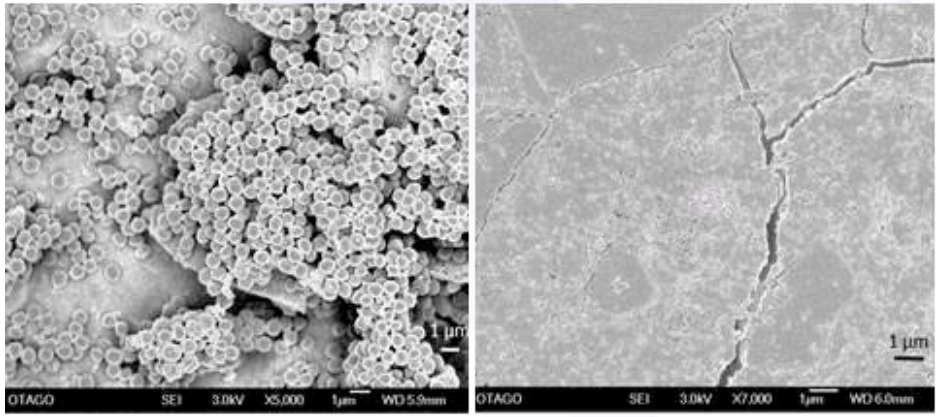


- Morphology assessment (SEM)
- Fluorescence-based viability assay (CLSM)

Unmodified Fuji IX

Ag NP-modified Fuji IX (6 µg Ag)

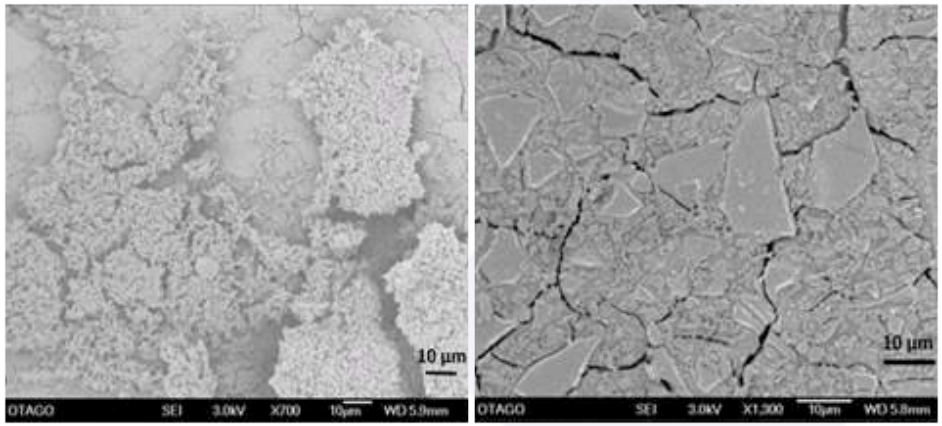
Strep.sanguis



Unmodified Fuji IX

Ag NP-modified Fuji IX (6 µg Ag)

Strep.mitis



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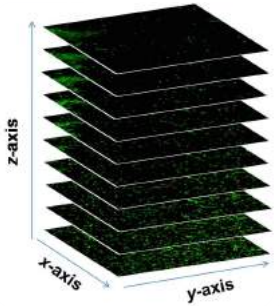
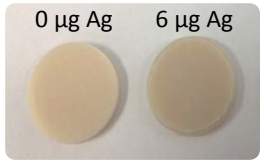
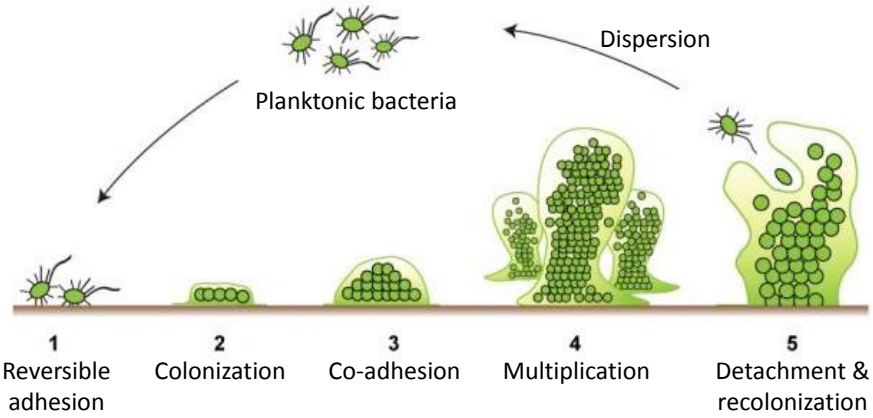
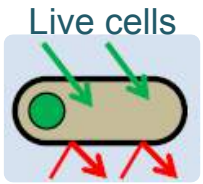


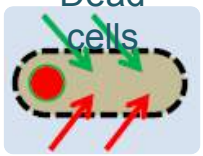
UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

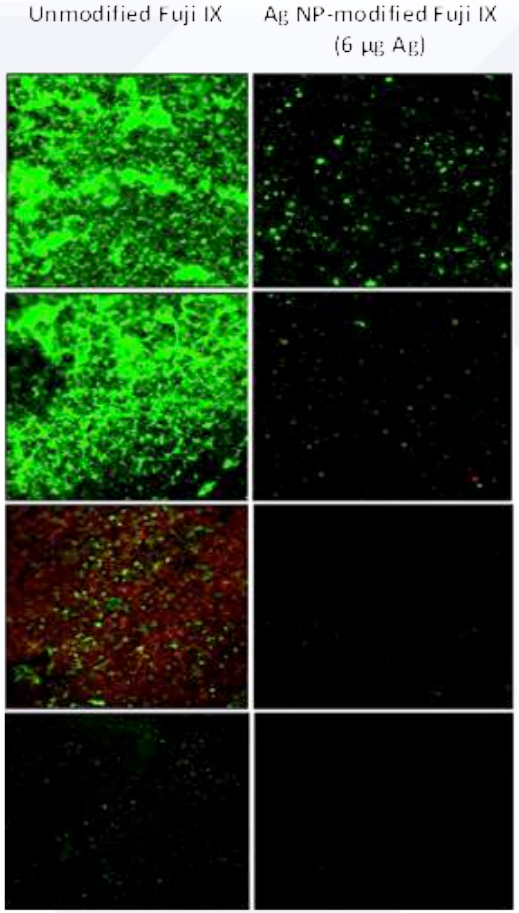
silventum





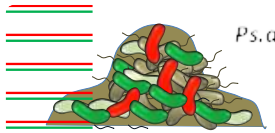




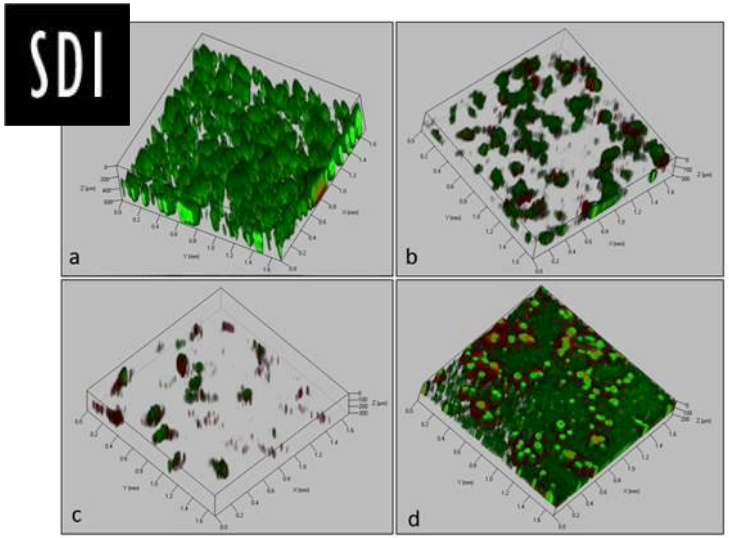


Morphology assessment (SEM)

Fluorescence-based viability assay (CLSM)

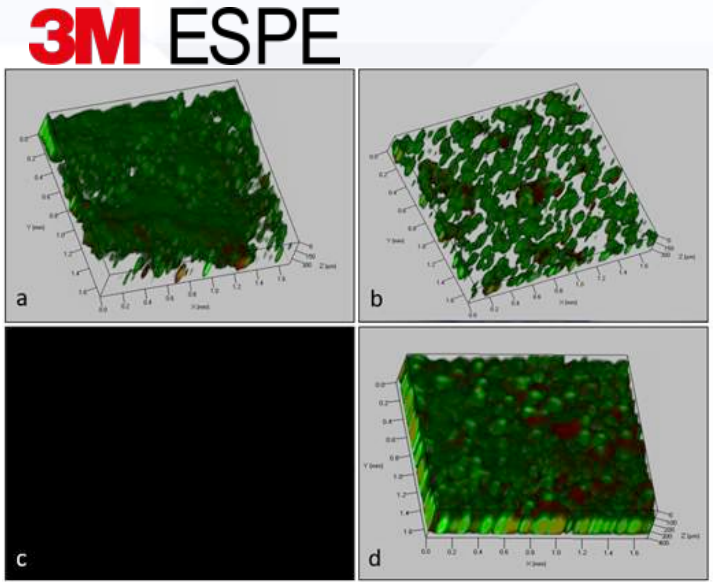


Antimicrobial activity of GICs: biofilm prevention



CLSM images of *S.mutans* biofilms grown on the surface of:

(a) unmodified commercial GIC,
(b) Ag NP-modified commercial GIC (Ag = 10 µg),
(c) Ag NP-modified commercial GIC (Ag = 24 µg),
(d) GIC manufacturer's silver-GIC (Riva Silver).



biofilms grown on the surface of:

(a) unmodified commercial GIC,
(b) Ag NP-modified commercial GIC (Ag = 10 µg),
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(d) GIC manufacturer's silver-GIC (Ketac Silver).

Mechanical properties of GICs

Manufacturer	GIC Sample	Compressive Strength / MPa	Flexural Strength / MPa
GC	Unmodified Fuji IX	195.09 (47.75)	14.60 (6.01)
GC	Ag NP-modified Fuji IX (Ag = 6 µg)	194.50 (38.95)	15.65 (6.24)
GC	Ag NP-modified Fuji IX (Ag = 10 µg)	215.81 (22.53)	15.58 (4.44)
GC	GC Miracle Mix	97.85 (26.72)	8.37 (1.67)
SDI	Unmodified GIC	205.88 (58.34)	27.12 (11.18)
SDI	Ag NP-modified GIC (Ag = 10 µg)	212.45 (46.63)	
SDI	Ag NP-modified GIC (Ag = 24 µg)	233.65 (26.23)	43.69 (12.33)
SDI	Riva Silver	158.54 (29.97)	27.41 (6.99)
3M-ESPE	Unmodified GIC	209.45 (28.85)	38.43 (10.23)
3M-ESPE	Ag NP-modified GIC (Ag = 10 µg)	238.20 (37.28)	
3M-ESPE	Ag NP-modified GIC (Ag = 24 µg)	214.88 (46.76)	38.84 (11.85)
3M-ESPE	Ketac Silver	188.45 (26.94)	30.54 (8.25)

Silventum Limited

Silventum Ltd is a recent spin-out company from the University of Otago set up to commercialise innovative dental materials that will reduce decay and extend the lifetime of natural teeth and dental implants.

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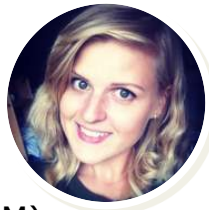

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