"Introduction to Water Purification"

The Park Hotel, Chiangmai

June 11th, 2013

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Today's Agenda

- ✓ Water Contaminants
- ✓ Water Quality Monitoring
- ✓ Water Purification
- ✓ Water Standards

Why is water important to scientists?

Because water is:

an excellent solvent, abundant, available, non toxic

water is the most widely used reagent

good at heat transfer (cooling / heating applications).

deeply linked to biological processes

Pure water is required because:

- the presence of contaminants
- the fluctuation of the purity

…can greatly impact the results of scientific experiments

Merck Millipore Lab Water Systems History

1969

The Super-Q

The 1st Millipore water purification system.

A bowl-containing-filter concept, delivering ultrapure water quality at relatively high flow rate. System more appropriate to pilot scale than lab scale.

1973

- **The Milli-Q**

1st generation. It includes recirculation pump - Meg-O-Lite technology for resistivity test - Twin 90 (0.22µm) end filter

- **Milli-*Q3*** :The 1st Millipore Reverse Osmosis (RO) system !

It includes a prefilter + RO membrane + 55 L reservoir, in a cabinet.

1989 : The compact range !

Compact - Bench or Wall mounting - Pack concept - Digital Display

- **Milli-Q Plus 6th generation:**

Q-Pak (3 types related to feed water quality) – model with UltraFilter– model with UV at 185/254nm (1991)

- **Milli-RO 6 / 10 and 6 Plus / 10 Plus**

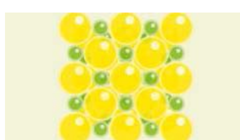
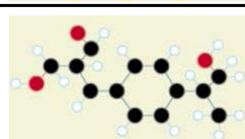
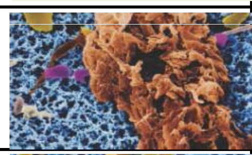
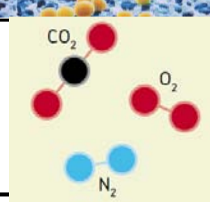
The "Plus" means: 2 conductivity cells added before and after RO membrane for quality measurement

ROPAK containing polyphosphate (= no softener needed)

Milli-Q Century range (2001)

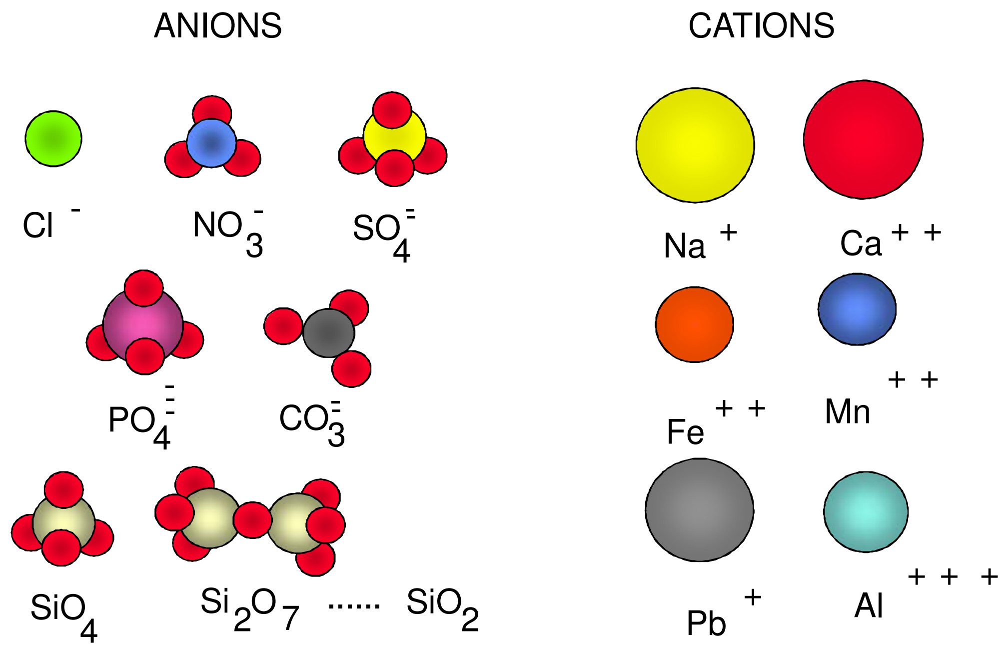
Elix Century range (2001)

Water Contaminants

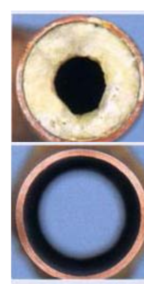
Inorganic Ions		**Cations** Na+ Ca+2	**Anions** Cl- HCO-3
Organics		**Natural** Tannic Acid Humic Acid	**Man Made** Pesticides Herbicides
Particles (Colloids)		**Non Dissolved Solid Matter** (Small deformable solids with a net negative charge)	
Microorganisms (Endotoxin)		**Bacteria , Algae , Microfungi** (Lipopolysaccharide fragment of Gram negative bacterial cell wall)	
Gases (dissolved gases)		N_2, O_2, CO_2	

MINERAL (Salts)

Common salts in natural water



Specific Inorganic Ions of Interest

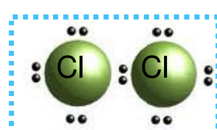


Calcium & magnesium (Ca^{2+} & Mg^{2+}) = hardness

- Association with carbonate to form a solid precipitate = <u>scale</u>
  → hard deposit on system parts (e.g. RO membrane, valves…)

CO_2 *(see "Dissolved Gasses")*

- Produces carbonate then favors scaling
- → acidic pH when dissolved into pure water



Chlorine

- Added to tap water to limit bacteria growth

→ pierces holes into the RO membrane

Alkalinity (mainly sum of carbonates & hydroxyl)

- → basic pH which favors scaling

Silica

- Average retention on purification media → possible breakthrough as thin dust
- Detrimental to machines directly fed by water system (Clinical analyzers, weather chambers..)

Water Hardness - Definition

Hardness measures the amount of Calcium and Magnesium
⇨ it represents the ability of water to form scale.

Scale = a <u>solid mineral deposit</u> which is detrimental to water purification equipment such as reverse osmosis and continuous deionization devices.

Temperature impact :

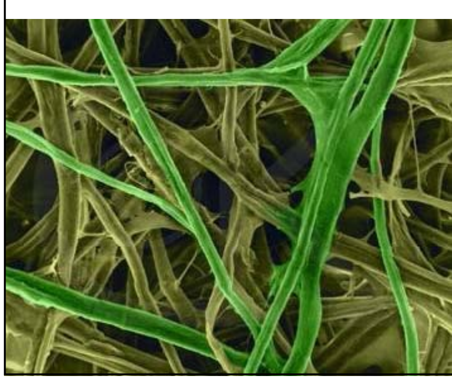
- Water temperature increase favors scaling

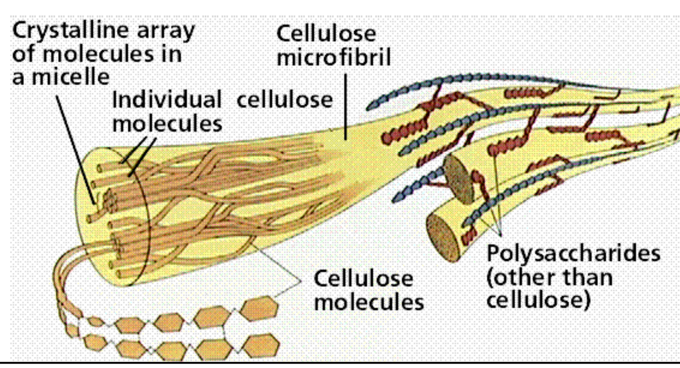
pH impact:

- Basic pH favors scaling

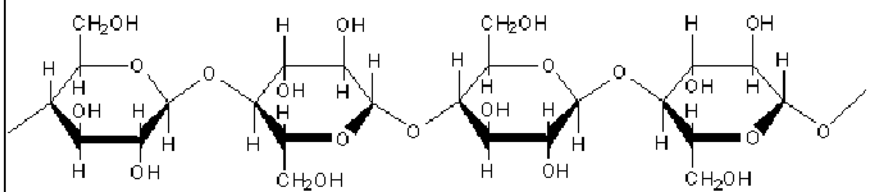
ORGANICS

Organic Solutes (natural origin)

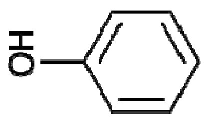




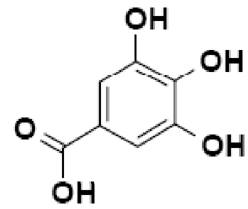
Organic Solutes (Natural origin)



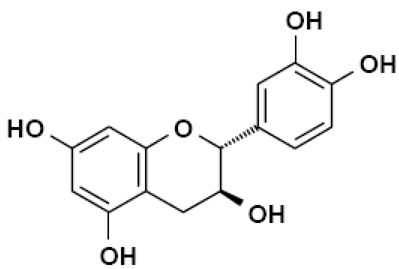
Cellulose



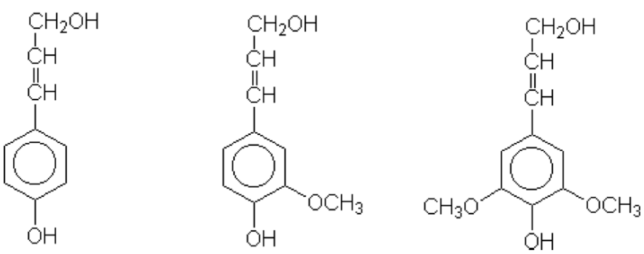
Phenol



Gallic Acid



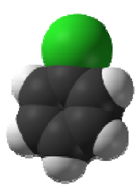
Catechin (a tannin or polyphenol)

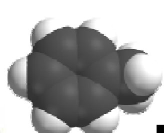


Lignin Monomers

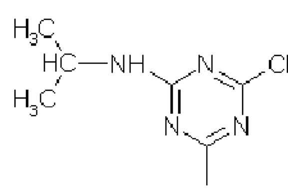
Organic Solutes (Artificial Origin)

VOC

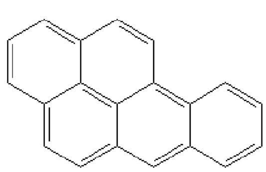




Pesticides

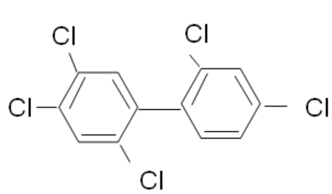


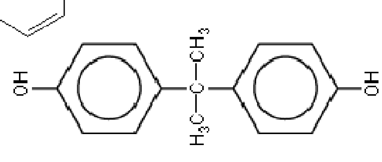
PAHs

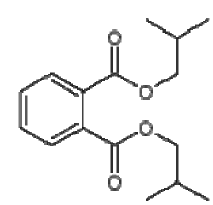


Plasticizers

PCBs



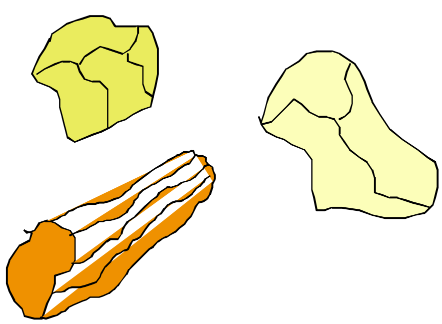




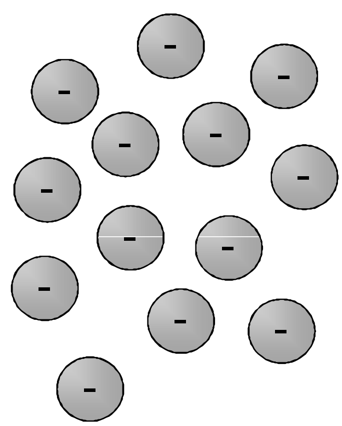
Effects of organics on lab experiments

- Dissolved organic contaminants can acts as complexants and "hide" ions when elemental analysis is performed, especially at lox levels (ppb & sub ppb)
- Some organics will interfere with organic reactions
- Dissolved Organics in water will affect chromatography separations causing the following issues
  - Loss of sensitivity (due to competition to bind sample on solid phase)
  - Loss of resolution (due to mass transfer issues)
  - Shorter column life time (due to mass transfer issues)
  - Unstable baseline
  - Ghosts peaks (contaminants visible at detection wavelength)
- Organics may interfere with biochemical analysis – for instance, humic acids are known to affect PCR tests

Particles and Colloids



Hard or Soft Particles : size above 100 nm (0.1 µm) – in suspension in water

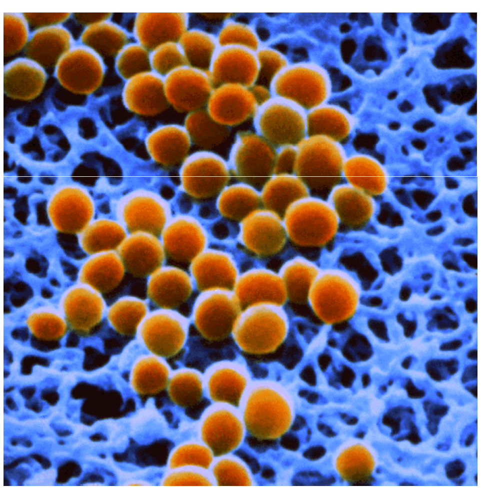


Colloids: inorganic or organic Electrically charged particles with size between 1 and 1000 nm

Effects of Particulates on lab experiments

- Particulates can affect delicate laboratory instruments: plugging tubing or protection frit, preventing valves to operate properly, plugging holes…
- Particulates interfere in particulate analysis, slides staining processes, microcopic observation procedures
- Particulates act as a support for bacteria and help them develop
- Particulates & colloids will interfere with spectrophotometric detection
- Particulates & colloids in water used as mobile phase in chromatography will damage pump heard, plug columns
- Colloids have a high developed surface and can affect organic or mineral synthesis reactions, causing variability and lack of experimental reproducibility.
- Colloidal silica in water biases the results delivered by weatherometers

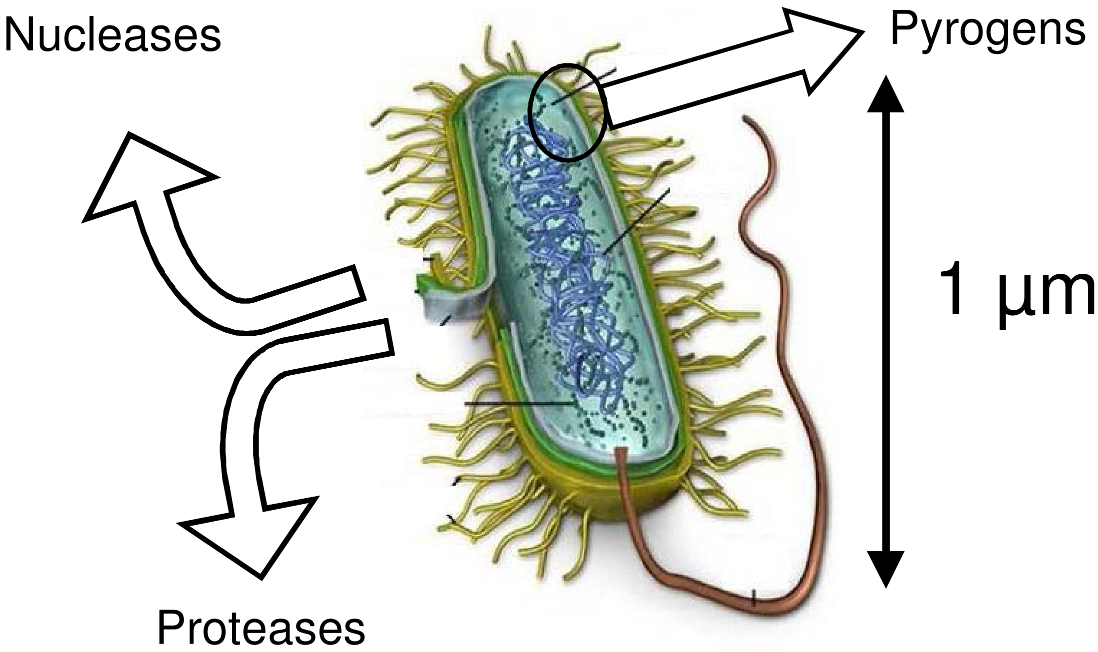
Bacteria



Staphylococcus Aureus

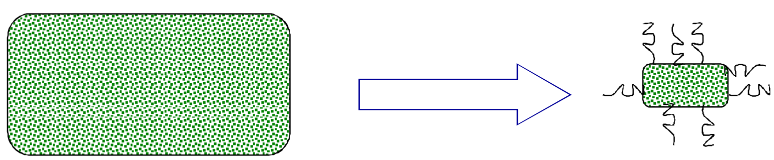
Serratia Marcescens

Bacteria By-products

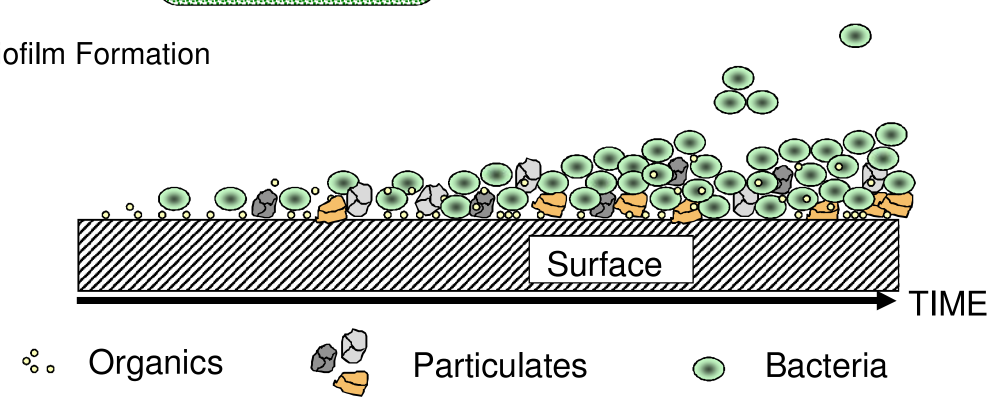


Adaptation to Pure Water

- Bacterial size reduction: 10µm to 3µm for better nutrient use,
- Exo Polysaccharide chains coating for sticking on surfaces.



- Biofilm Formation



How to remove bacteria ?

Chemical sanitizing agents: H_2O_2, $NaHClO_3$…

- Most common = sodium hypochlorite (NaClO), used in tap water (1 to 3 ppm).
- Chlorine released → bacteria death.
- Benefits : Well known, easily available, easy to use, cheap.
- Limitations:
  - chemical contamination of the water to be removed ; then test water for residues detection down to a low limit.
  - Not very efficient against biofilms.
  - new organic contaminants in the water: bacteria cell + cell content, new compounds formed by reaction with other chemicals maybe toxic (e.g. organochhlorine).

UV radiation at 254 nm

- Used on-line with the produced purified water flow.
- Irradiation of purified water stored in the tank.

Microfiltration membranes (0.22µm)

PYROGENS

Pyrogen Characteristics

= endotoxins (toxins from the inside of the bacteria),

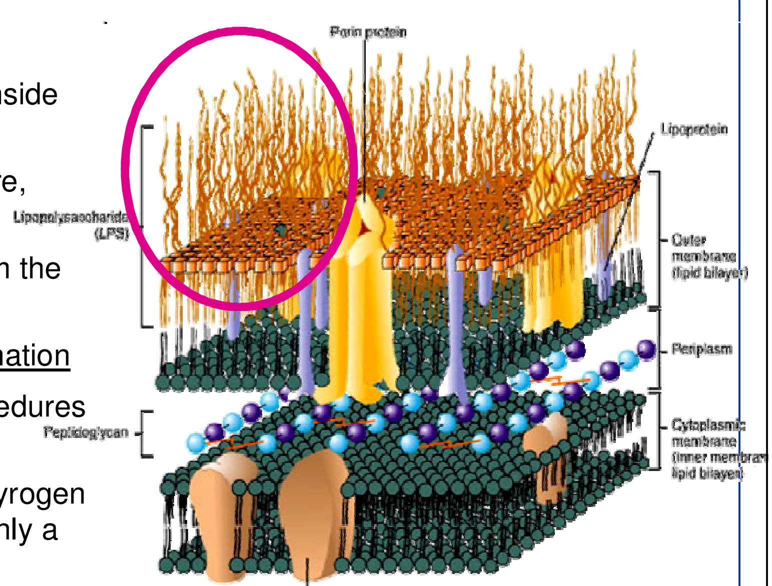
Named from Greek “pyros” = fire, because induce fever.

= LPS *(lipopolysaccharide)* from the wall of bacteria Gram –

→ Indicate a bacterial contamination

Resistance to autoclaving procedures (3h at 121°C)

Exposure for 4h at 180°C → pyrogen concentration reduced by only a factor 1,000 (LRV = 3).



Pyrogens Removal

Ultrafiltration (UF) membranes with the right cut-off do not allow pyrogen passage. → pyrogen free water.

Charged membrane filters (such as Durapore cartridges) have been qualified for the removal of pyrogens.

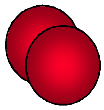
Oxidizing agents (ozone, hydroxyl radicals) generated by a UV lamp break down endotoxins (because organic) very efficiently.

Effects of Bacteria on lab experiments

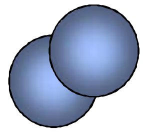
- ❖ Bacteria in water are a nuisance in bacteriological analysis labs
- ❖ Bacteria present in water used to produce culture media or buffers for cell culture will eat up the nutrients designed for cell development
- ❖ Bacteria may develop inside lab instruments and produce a biofilm on the surfaces, creating instrumental issues.
- ❖ Dead Bacteria generate many by-products that can cause issues
  - ❖ Low Molecular Weight Organics
  - ❖ Ions
  - ❖ Pyrogens that affect cell culture & molecular biology experiments
  - ❖ Nucleases (RNases & DNases) which affect PCR or DNA sequencing
  - ❖ Proteases

DISSOLVED GASES

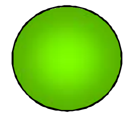
Gases



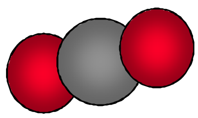
Oxygen



Nitrogen



Radon



Carbon Dioxide

Dissolved Gases

Common gases dissolved in water = air gasses

Air main gases: Nitrogen (N_2 ~80%), Oxygen (O_2 ~20%), Argon (Ar ~1%), Carbon Dioxide (CO_2 ~0.03%)

Gas behavior when in contact with water:

- Gas remains the same molecule but dissolved in water - e.g. oxygen
- Gas interacts with water molecules to form other molecules
  e.g. chlorine Cl_2 → hypochlorous acid (HClO) & hypochlorite (ClO)

CO_2 behavior: $dCO_2 + H_2O \Leftrightarrow \underline{H_2CO_3} \Leftrightarrow HCO_3^- + H^+ \Leftrightarrow CO_3^{2-} + 2\,H^+$

→ 4 existing forms in equilibrium with a higher level of bicarbonate

→ production of H^+ → pH decrease in pure water

Temperature impact: T° increase → **less** gas dissolves into water

Pressure impact: P increase → **more** gas dissolves into water

Effects of Gases on lab experiments

- Dissolved gases may cause issues in some specific analytical techniques.
- Some reactions require dissolved oxygen to operate and will be affected by its concentration in water.
- When water is heated, the solubility of dissolved gases decreases, and air bubbles appear. These bubbles will cause issues such as, for instance, disturbing a photometric measure. This is a well known issue in clinical analyzer which require feed water with low dissolved gases.
- The USP also requires to use low dissolved gases water in some applications, such as dissolution testing.

Conclusion

- Natural water contains 5 main classes of contaminants
- These contaminants, if they may have negative effects on human health, are removed down to a safety level by Water Companies
- Potable tap water still contains some of these contaminants, at levels that are not harmful for humans
- However, even at that level, these contaminants can be detrimental to laboratory instruments & experimentations
- These contaminants should therefore be monitored and removed to acceptable levels by appropriate techniques.
- When their effect on experimentation is unknown, they should be removed as much as possible (precaution principle)

Monitoring Tools

Water Quality Monitoring

Measurement of Contaminants

Contaminants	Measurement	Unit
Inorganic Ions	Conductivity (Resistivity)	µs/cm MΩ.cm
Organics	Total Oxidizable Carbon (T.O.C.)	ppb (µg/L)
Particles (Colloids)	Silt Density Index / Fouling Index	Rate of pluggage of 0.45 µm membrane.
Bacteria	Colony count on 0.45 µm Membrane.	cfu/ml
Endotoxin	Rabbit Inoculation test LAL Test	Endotoxin units/ml

Conductivity measurement

Conductivity and resistivity are used to define the overall ionic purity / contamination

Conductivity

$$X = F\sum c_i z_i \mu_i$$

- X: Conductivity (Siemens/cm)
- F: Faraday constant
- c_i: Concentration of each ionic species (eq/ml)
- z_i: Valence
- μ_i: Mobility $\Omega^{-1}.cm^{-1}.s^{-1}$

$[H^+] = [OH^-] = 10^{-7}$ M

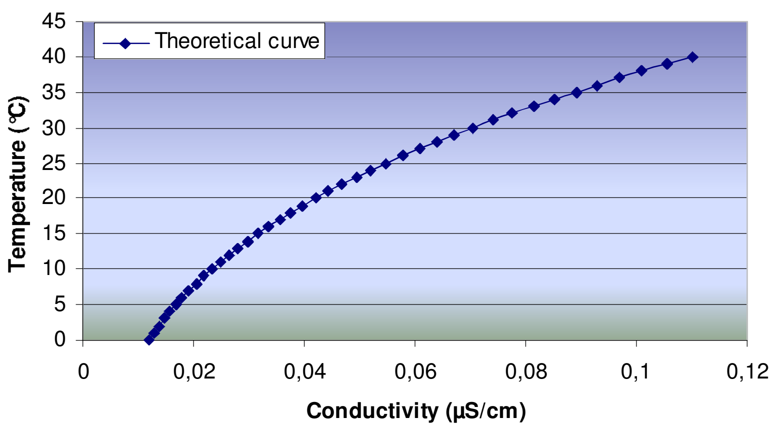
Minimum theoretical conductivity is 0.055 µS.cm^{-1} *at 25 °C*

Resistivity

$$R = \frac{1}{X}$$

Maximum theoretical resistivity is 18.2 MΩ.cm *at 25 °C*

Effect of Temperature on Conductivity



Standard: report conductivity/resistivity @ 25 °C

Conductivity and Ions Concentration

NaCl (ppb)	Conductivity (µS/cm)	Resistivity (MΩ.cm)
0	0.055	**18.20**
1	0.057	17.6
5	0.066	15.2
10	0.076	**13.1**
20	0.098	10.2
50	0.16	6.15
100	0.27	**3.70**
300	0.70	1.43
500	1.13	0.88
1,000	2.21	**0.45**

Calculated values for NaCl solutions at 25°C

(with concentration and mobility of proton, hydroxyl, sodium and chloride ions)

Resistivity of 18.2 MΩ.cm : less than 1 ppb of ions present in the water

Different Conductivity Cells - Millipore

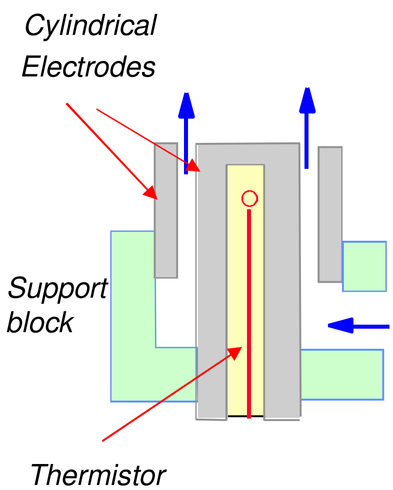
Tap water (0.3 cm^{-1})

RO permeate (0.12 cm^{-1})

Type I & II water (0.01 cm^{-1})

Flow-through Coaxial Resistivity Cell

The Millipore Resistivity Cell



Concentric electrodes :

Design ensuring reproducible manufacturing and stable cell constant.

High quality 316 L stainless steel

Low cell constant : 0.01 cm^{-1}

→ very good accuracy even at low resistivity (UPW) .

No dead legs : immediate response, real resistivity.

Thermistor :

Protected inside the electrode
Sensitivity 0.1 °C

pH of Pure Water

In pure water: $[H^+] = [OH^-] = 10^{-7}$ $mol.L^{-1}$ → **pH = 7**

Measurement problems with conventional pH meter:

- Pickup of CO_2 from the air (addition of H+ in water -> pH decrease)
- Creation of an electrical parasite at the water / electrode interface on the reference electrode (not enough ions)

Solutions :

- Measuring in line after dissolution of neutral salt (KCl) – *difficult* !
- Measuring the resistivity – NOT the pH ! (cf. *Monitoring Tools*).
  Note : the resistivity varies with the amount of ions in the sample

A resistivity of 18.2 MΩ.cm is a guarantee of a pH=7 at 25°C.

TOC Concept

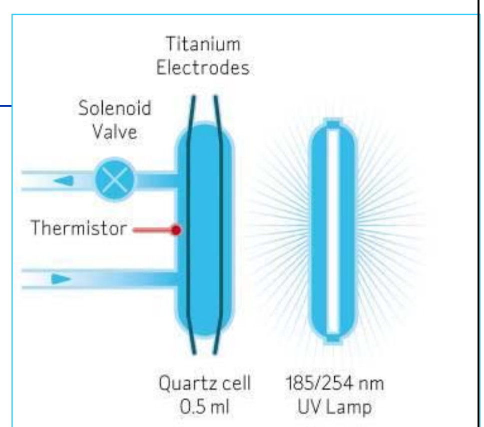
TOC = Total Oxidizable Carbon (or total organic carbon)

Tap water may contain hundreds of different oxidizable carbon substances at different concentrations.

TOC measurement is a way of normalizing the amount of organic carbon containing compounds in water.

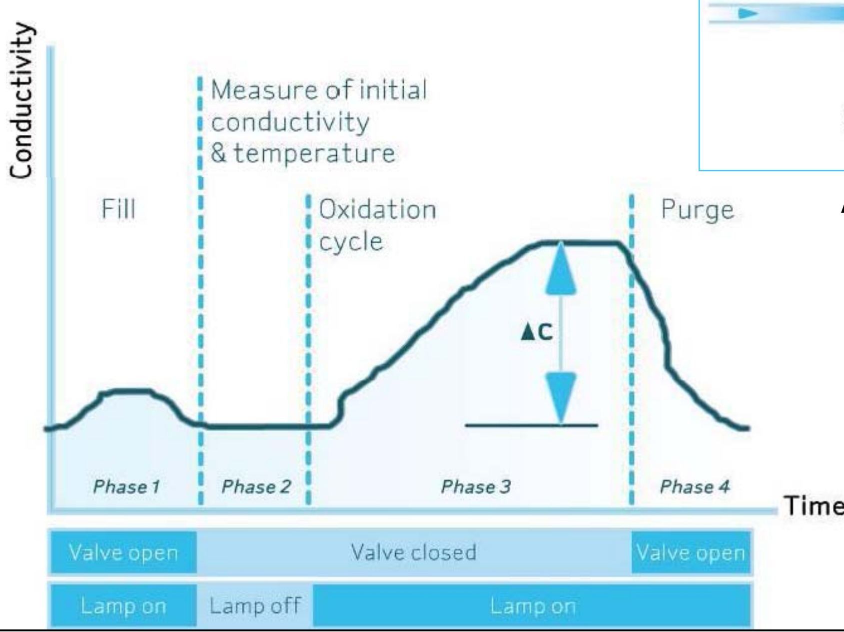
TOC monitoring expresses the total organic contamination of water with a single figure thanks to the UV photooxidation reaction.

TOC Monitor Functioning



A10 TOC Monitor

Measuring cycle



Why measure the TOC?

- Organic purity affects experimental results
- TOC is measured as an indicator of water quality or cleanliness
  - In the environmental field (natural / waste / drinking water)
  - In Pharma (for manufacturing equipment….)
  - In Food and Bev (safety…)
- TOC used to monitor environments, processes for safety and efficiency (e.g semiconductors, petroleum)

So far only ionic contamination was monitored (conductivity)…

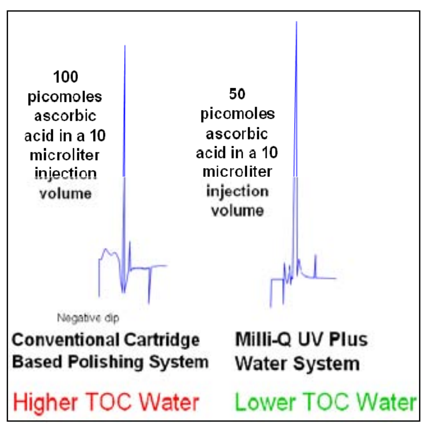
Now international standards require
more and more low TOC values for ultrapure water.

TOC - Academic & Research Markets

Laboratory Grade Water Norms also use TOC

Norm	Type 1	Type 2	Type 3
ASTM	< 10	< 50	< 200
ISO 3696	NA	< 80	< 200

High TOC effects in LC
- ❑ Less sensitivity
- ❑ Loss of resolution
- ❑ Shorter column life
- ❑ Baseline issues



Millipore was the first company to provide laboratory water systems with TOC values (1994)

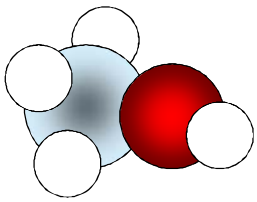
Conclusion

- The value of TOC is a measure of the carbon content coming from organic molecules in a solution
- Different organics will deliver slightly different TOC values because the carbon content of these organic molecules is different
- But all organic molecules will contribute to the TOC value as they are all made of carbon atoms.
- Therefore, the measure of TOC is a quick way to evaluate the level of organic molecules concentration in water
- The TOC measure is actually well adapted to check a low organics contamination, just like resistivity allows to check a low ionic contamination in water.

Merck Millipore and TOC measure

- A Merck Millipore Stand alone TOC monitor made by Anatel was introduced in 1994 – Anatel had developed a key patent for TOC monitoring: oxidation and measure of conductivity performed in the same cell.
- In 1996 range, Millipore signed a contract with Anatel and introduced the built-in TOC monitor in Millipore Lab Water Systems – with limitation to 250 ppb upper detection level
- In 2001, with the Century range launch, improvements allowed us to measure TOC up to 999 ppb and to perform suitability tests.
- In 2005 we developed our own TOC monitor using the license from Anatel. We are now developing, manufacturing and calibrating our own TOC monitors

Methanol Solution: relation ppb & TOC



Methanol
CH_3OH

Molecular Weight (MW)

Atoms		Units	Weight	
C	Carbon 1	1 x 12 =	12	
H	Hydrogen	4	4 x 1 =	4
O	Oxygen 1	1 x 16 =	16	

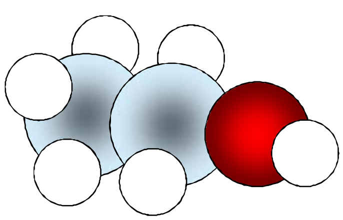
Methanol Molecular Weight 32

What will be the TOC level generated by a 50 ppb methanol concentration in pure water ?

The carbon content of methanol is 12 / 32 = 0.375

Therefore , **50 ppb** methanol solution generates
50 x 0.375 = **18.75** ppb TOC

Ethanol Solution: relation ppb & TOC



Ethanol
CH_3CH_2OH

Molecular Weight (MW)

Atoms		Units	Weight	
C	Carbon 2	2 x 12 =	24	
H	Hydrogen	6	6 x 1 =	6
O	Oxygen 1	1 x 16 =	16	

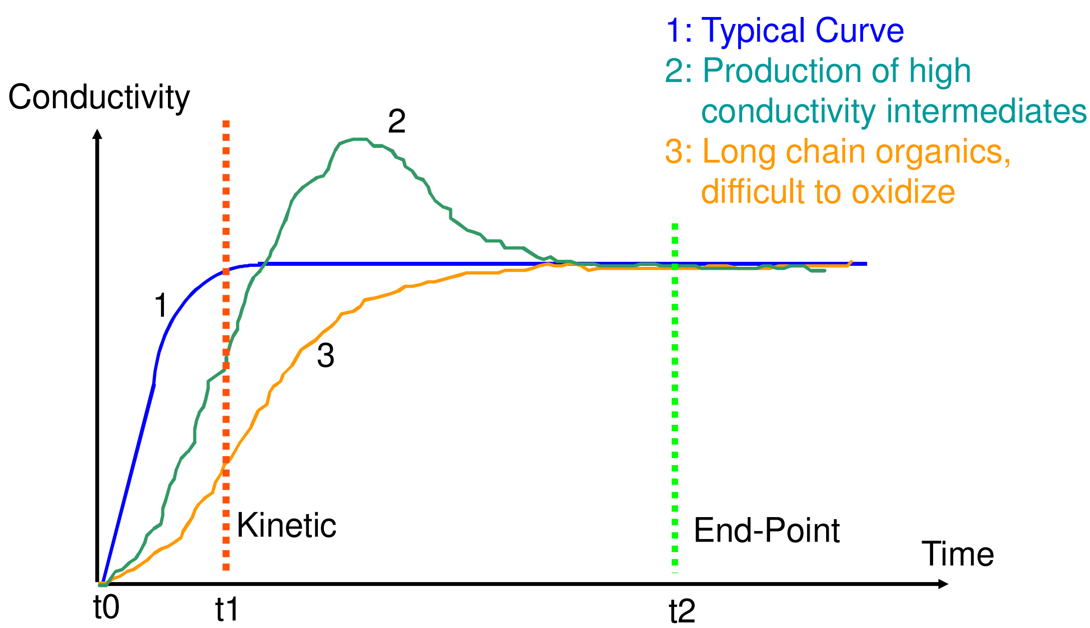
Ethanol Molecular Weight 46

What will be the TOC level generated by a 50 ppb ethanol concentration in pure water ?

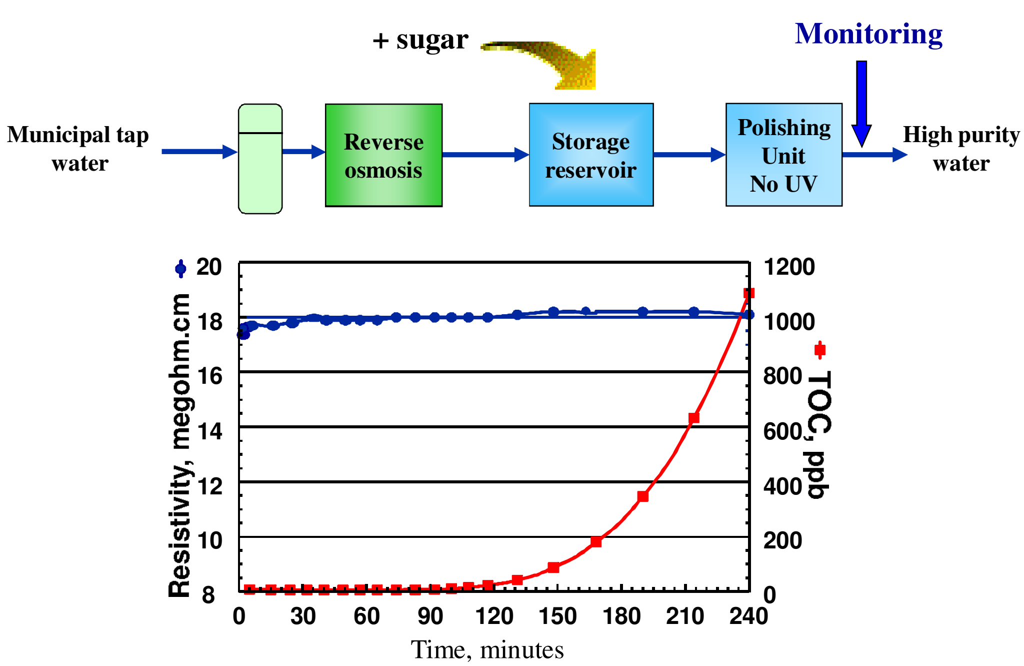
The carbon content of ethanol is 24 / 46 = 0.521

Therefore , **50 ppb** ethanol solution generates
50 x 0.521 = **26** ppb TOC

TOC: Kinetic vs End Point Test

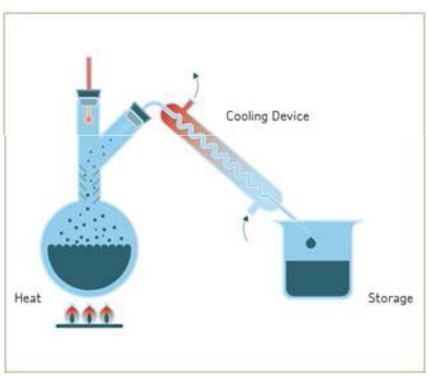


Absence of correlation between resistivity and TOC level in ultrapure water



Purification technologies

Distillation



Benefits

Removes a broad range of contaminants and therefore useful as a first purification step.

Reusable.

Limitations

Contaminants are carried to some extent into the condensate.

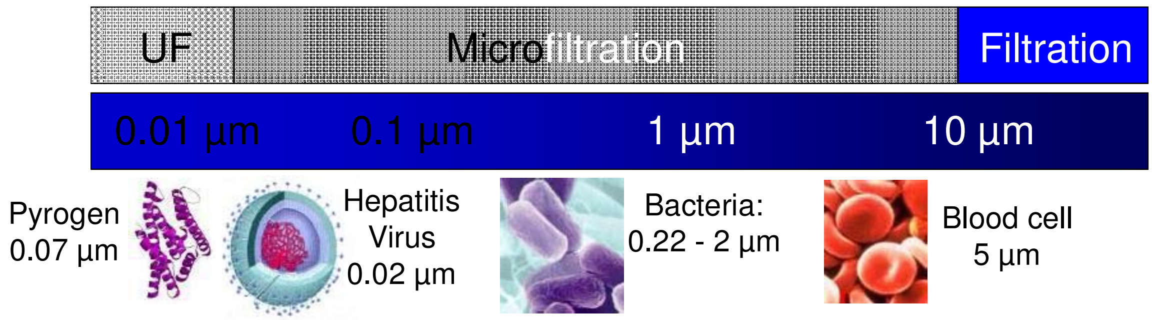
Requires careful maintenance to ensure purity.

Consumes large amounts of tap water (for cooling) and electrical energy (for heating).

Not environmentally friendly.

Microfiltration

Microfiltration is the removal of contaminants based on their size, typically in the field between 0.025 µm and 10 µm.



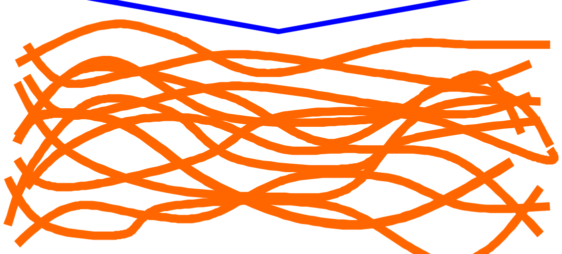
Microfilters are used in lab water purification for removal of particulates & bacteria

There are 2 types of microfilters: depth & screens

Depth & Screen Filters

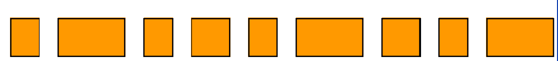
Depth Filters

Depth filters are usually made of fibers assembled together. A good image is a bush.

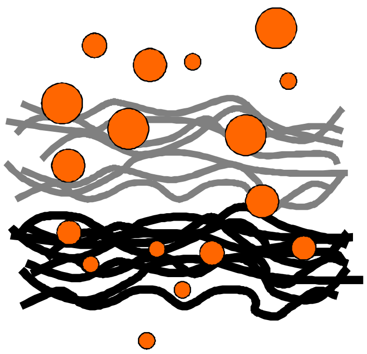


Screen Filters

Screen filters are like a sieve. Example: a plate pierced by holes of the same diameter or a net



Depth Filtration

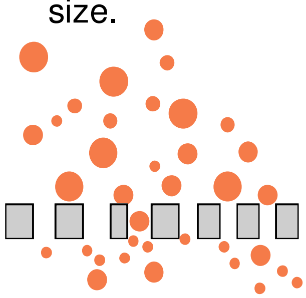


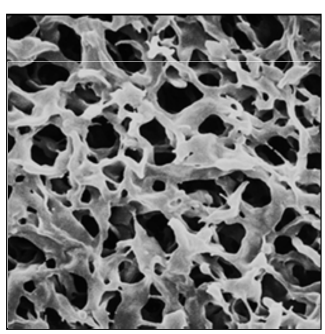
- Depth filter : particulates retention throughout the filter media, based on their average size.
- Used as pretreatment to protect RO membrane in Progards & Prepak

Progards 1 & 2

Absolute Filtration

- Screen filter : removal of 100% of contaminants which size is greater than membrane pore size.





Durapore membrane (electronic microscope)

- Main LW example: the MilliPak at the POU of Milli-Q.

Depth Filters vs Screen Filters

Depth Filters	Screen Filters
▪ High particle load capacity [illegible] surfa[illegible]d the [illegible] the [illegible]	▪ Defined pore size (checked by a non-destructive test prior to and after filtration) → 100% retention of contaminants larger than pore size.
▪ [illegible] pore size	▪ Very little adsorption of liquid
▪ Media migration [illegible] filtrate	▪ No media migration
▪ [illegible] of bac[illegible] [illegible] in the matrix	▪ No grow-through of bacteria if right pore size selected.
▪ Possible [illegible] amounts of liquid (expensive solutions)	▪ Low particle load capacity due to a retention on filter surface
[illegible] as a pre-treatment	→ Use as a polishing technique

Activated Carbon & Water Purification

Activated carbon (AC) = very small particulates with small pores inside → very important developed surface.

1,000 m² / gram

Activated carbon in LabWater applications :

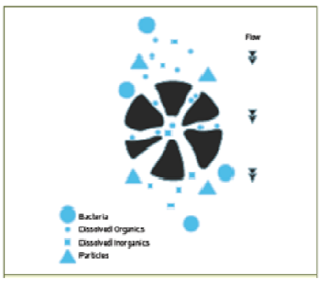
- Reduction of chlorine: as a protection for the RO membranes → Natural Activated carbon.
- Removal of organic substances by non specific binding (Van der Waals forces)
  - Some large organics in tap water absorbed by natural activated carbon of RO pre-treatment.
  - Small organics of treated water for ultra pure systems absorbed by synthetic activated carbon of polishing packs, including VOCs which are removed by a specific AC in Quantum VX)

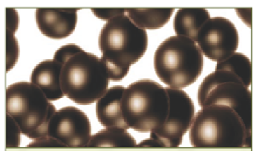
Activated Carbon

Benefits

❖Effective removal of a large range of organic substances (even of low molecular weight) by non specific binding (Van der Waals forces) or chlorine reduction

❖Large capacity due to high developed surface





Limitations

❖Very little effect on other contaminants (except some particulates removed by depth filtration)

❖Once all active sites are occupied, an equilibrium is established and organics are released.

❖Bacteria may develop after several months.

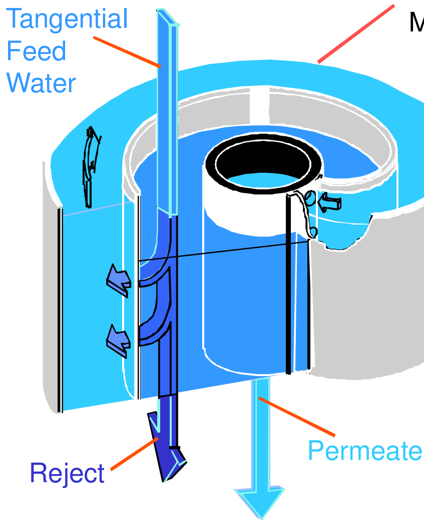
❖Efficiency depending on flow rate

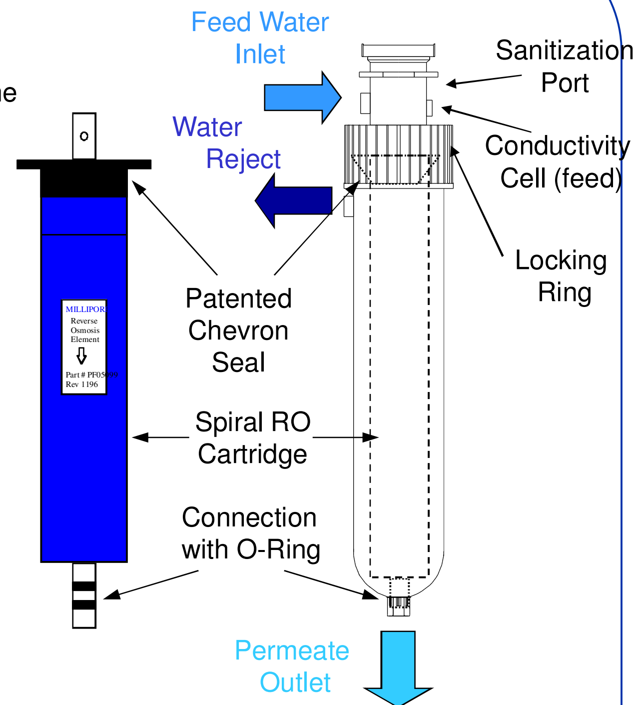
Reverse Osmosis

More than Filtration :

The Complete Purification Technology

Water Flow Path in Spiral Cartridge

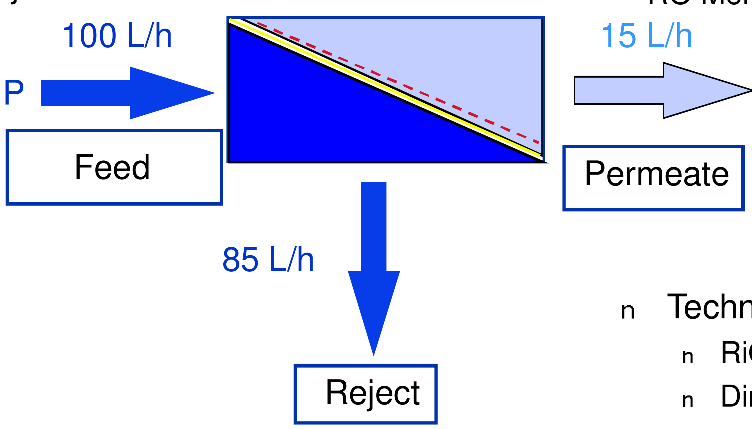




Reverse Osmosis

- Thanks to a pressure (P) 97% of the ions, 99% of the organics, particulates, bacteria & viruses in the reject

RO Membrane & housing



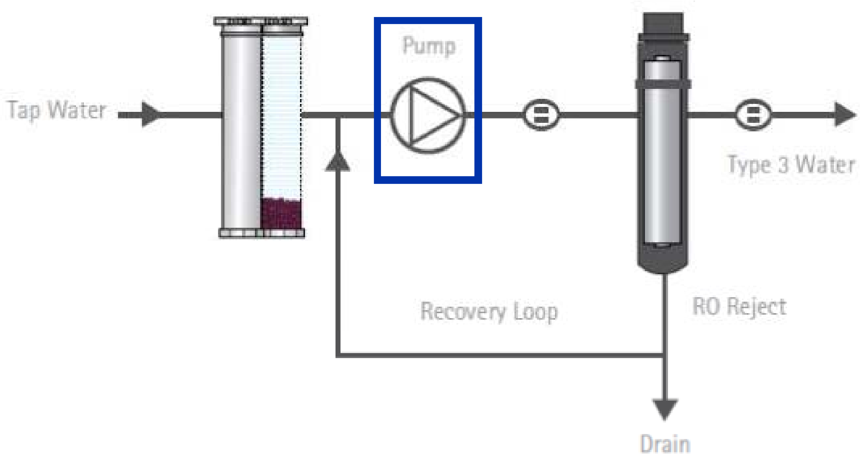
- Technology used in :
  - RiOs & Elix Systems
  - Direct-Q Systems

RO Technology :

- Tangential flow in order to limit fouling
- Remove 95 to 99% of inorganics
- Removes 99% of all dissolved organic substances (MW >200 Daltons), microorganisms, particles

Reliable, constant production of type 3 pure water

❸ Unique temperature control feature in the built-in booster pump



Constant Production via constant Flow Rate: The Intelligent RO

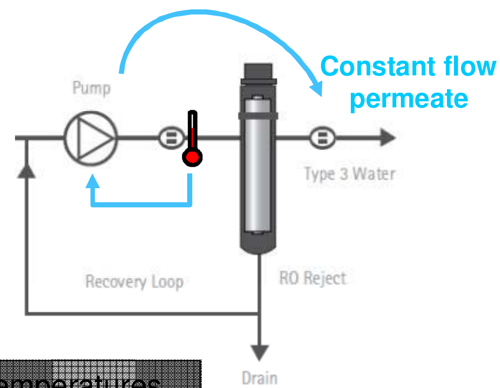
❶ **In traditional RO systems** permeate flow evolves proportionally with temperature:

T↓ flow↓ because of higher water viscosity

Ex: 6 L/h at 30°C → 2.5 L/h at 7°C

❷ **In RiOs, a controller…**

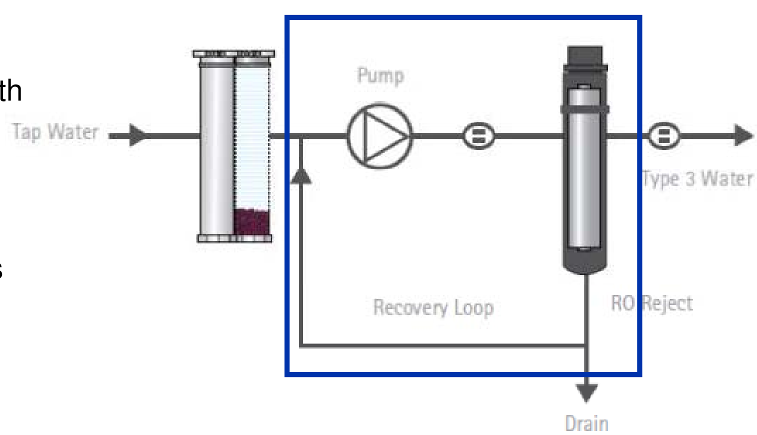
- checks feed water temperature
- adjusts pump voltage accordingly
    - to obtain the right pressure
    - for the permeate flow to be compensated



BENEFIT: constant flow rate at a range of temperatures

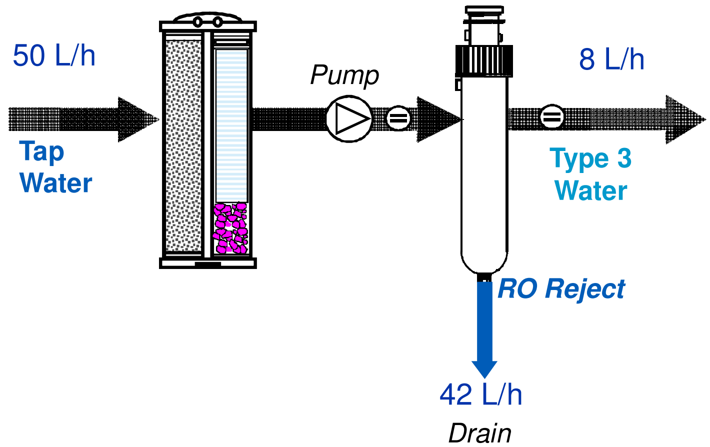
Low Running costs

- Advanced reverse osmosis technology with high recovery loop reduces water consumption by more than **50%**
- Recovery loop doubles the lifetime of the Pretreatment Pack
- Self maintenances functions and cleaning cycles ensure an extended RO membrane lifetime, and also an optimum final water quality



RO Recovery Loop

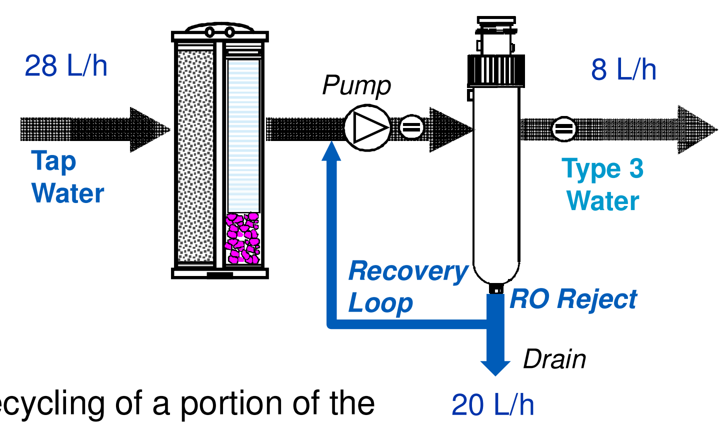
Rios 8 flows & recovery ***without*** reject recycling



RIOS 8 Recovery : 8/ 50 = 16 %

RO Recovery loop

Rios 8 flows & recovery ***with*** reject recycling



RIOS 8 recovery:
8 / 28 = 28.5%

- Recycling of a portion of the rejected water back to the RO membrane feed.

BENEFITS:
- Water savings
- Extended Progard life
- Reduction of running costs

Water Recovery of RiOs

SYSTEM	RiOs 5	RiOs 8	RiOs 16
Feed Water (L/h)	20	28	41
Reject Water (L/h)	15	20	25
Permeate Water (L/h)	5	8	16
Water recovery (%)	25	28.5	39

Reverse Osmosis Summary

Benefits

All types of contaminants removed (ions, organics - pyrogens, viruses, bacteria, particulates & colloids)

Minimum maintenance (good protection – Progard, automatic flush, semi-automatic cleaning & sanitization)

Ideal protection for polisher ion-exchange resin : a large ionic part already removed (↑ resin lifetime), particulates, organics, colloids also eliminated (no fouling).

Limitations

Type III water (limited ionic removal)

RO membrane sensitivity to

- *contaminants*: particulates plugging, organics & colloids fouling, piercing (particle, chemical attack) and scaling
- *back pressure* if not properly protected.

Need of right pressure (5 bars) & right pH for proper ion rejection.

Flow fluctuation with temperature if no compensation

Optimized reject needed

Storage required

Ion-Exchange Basics

Goal of the ion-exchange resin

- to collect contaminating ions in water

Action of the ion-exchange resin

- Removal of positive ions and negative ions separately by 2 different resins.
- Each resin specific to the ion charge.

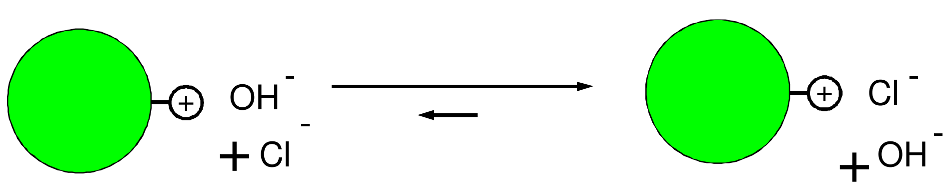
Composition

- Ion-exchange resins = large amount of tiny synthetic beads

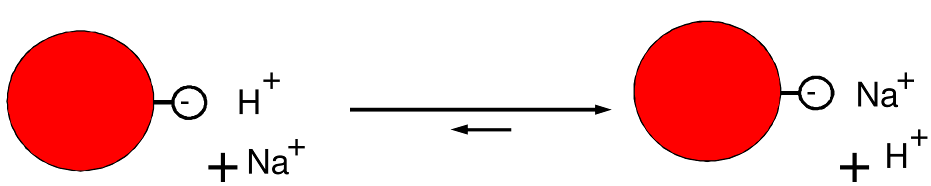
Ion-Exchange Reaction

Active Groups

Anion Exchange : remove anions (= ions that move towards the positive anode = negatively charged ions)



Cation Exchange: remove cations (= ions that move towards the negative cathode = positively charged ions)

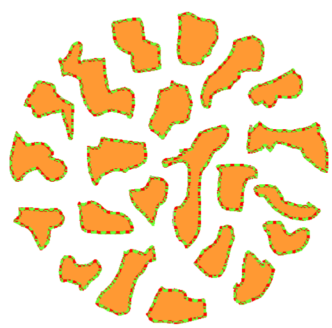


Mixed Bed Process

Benefits

Effective ion removal
→ Resistivity : 1-10 MΩ.cm in a single pass through the resin bed.

Easy to use : simply open the tap and get the water.



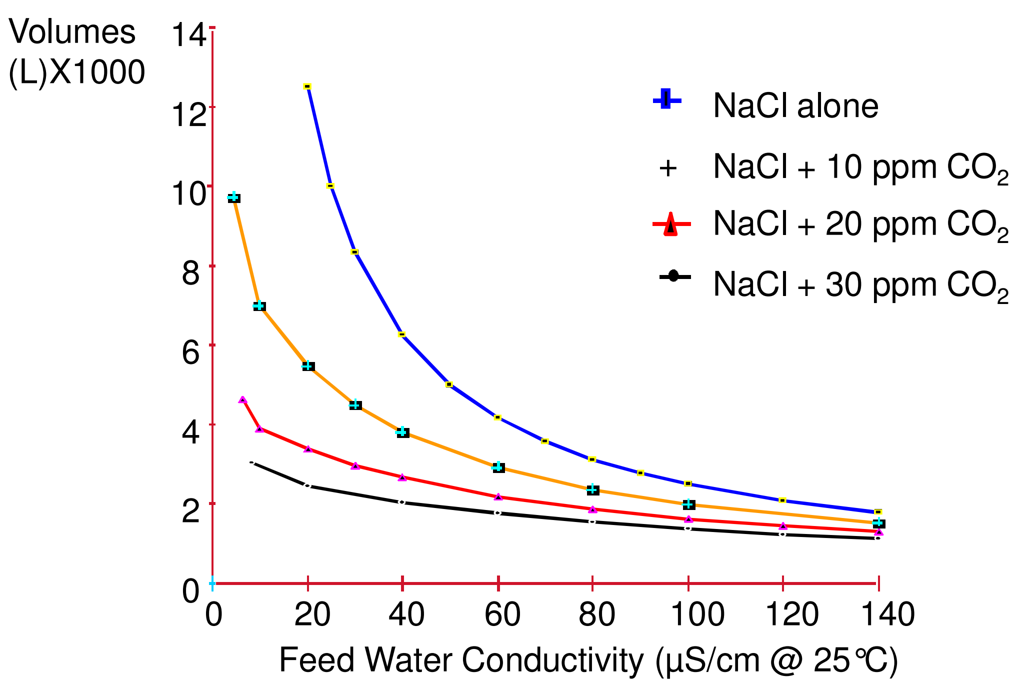
Limitations

No particles, organic materials or microorganisms removal

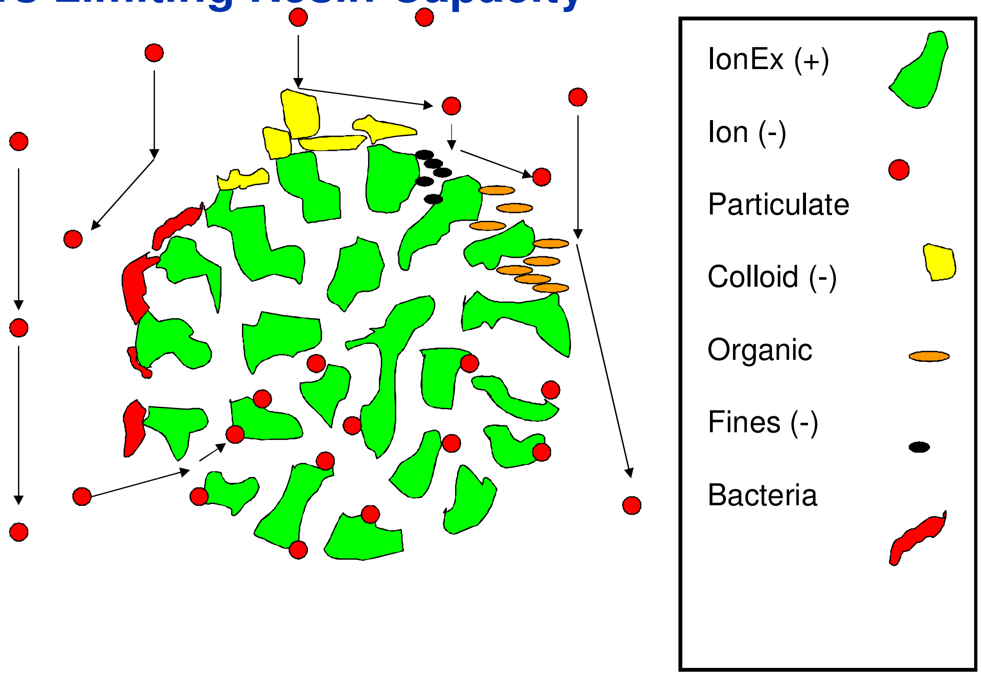
Capacity related to flow rate.

Incorrect resin selection or multiple regeneration will cause water contamination by organic and particulates.

CO_2 & Ion-Exchange Capacity

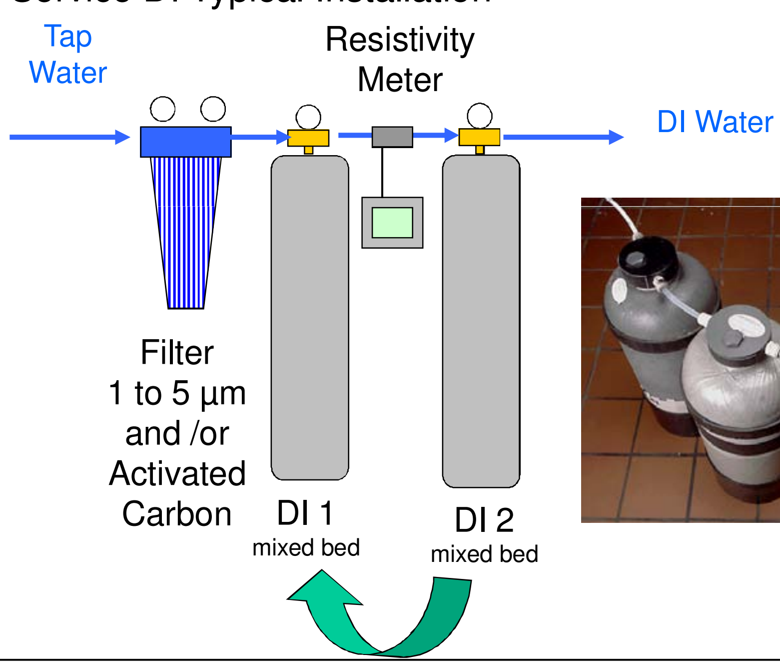


Factors Limiting Resin Capacity



Utilizations : Regenerable Service DI

Service DI Typical Installation



Service DI Summary

Benefit **:** Simple to install / Reliable (2 bottles) / Limited investment / Regenerable.

Inconvenient : **Water quality**

- High organic & particle contaminants ← tap water, bacteria, resin beads broken after multiple regeneration. Quality varies a lot from bottle to bottle.
- High bacteria development promoted by damaged beads.
- Potentially contaminated beads with heavy metals from previous usage (standard exchange: origin of resin unknown).
- Resistivity drop when Service DI nearly exhausted.
- Quick resin capacity decrease by organic fouling.
- Resin fine release → poison the rest of the beads and the high quality, single use ion-ex. resin of the water polisher

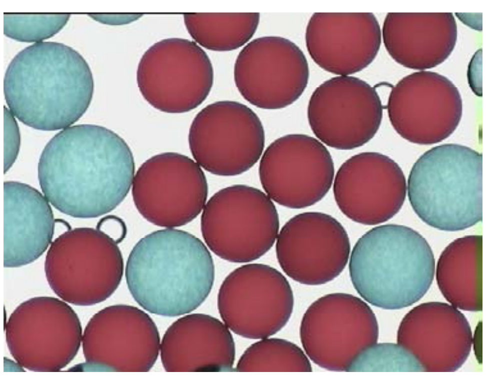
High running cost

- Regeneration + tranportation cost.
- Imperfect regeneration + organics → resin lower capacity

Q-Gard & Quantum resins

Characteristics:

- Size and color homogeneous,
- No particulates or fines,
- No cracked bead (single regeneration).



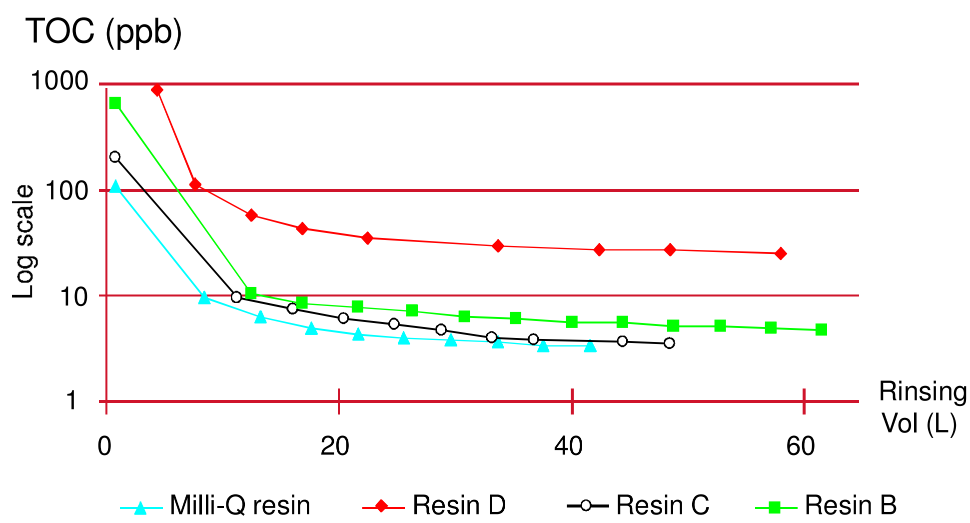
As a result:

- High capacity with good binding kinetics,
- Low organic release.

Millipore unique Jetpore® Ion-Ex resin

Organic Leakage of Resins

- TOC analysis of the rinsing water of various "nuclear" grade or "electronic" grade mixed bed resins.
- Rinsing water quality = ultrapure water - 18 mΩ.cm - 2 ppb TOC



ElectroDelonisation *(EDI)*

Definition:

EDI = continuous deionization technique where mixed bed ion-exchange resins are permanently regenerated by a weak electric current.

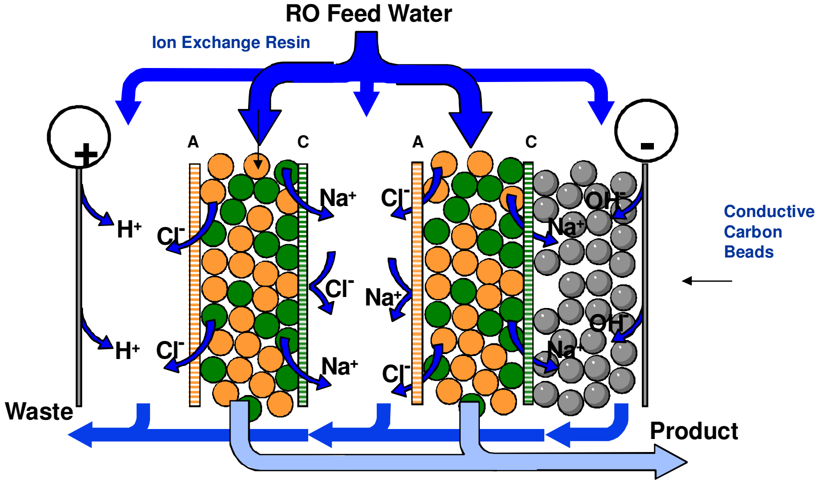
Association of electrodes with ion selective permeable membranes (developed by Millipore in the 80's) → efficient ion removal from water.

EDI feed water = RO treated water (NO tap water !)

→ avoid plugging, fouling, scaling of the module

The Continuous Deionization Purification Technology

Electrodeionization



EDI = continuous deionization technique where mixed bed ion-exchange resins are permanently regenerated by a weak electric current.

- Association of current with ion selective permeable membranes (developed by Millipore in the 80's) → efficient ion removal from water.
- EDI feed water: RO treated water
  → avoid plugging, fouling, scaling of the module

Scaling due to high pH at cathode

OH^- Generated at Cathode

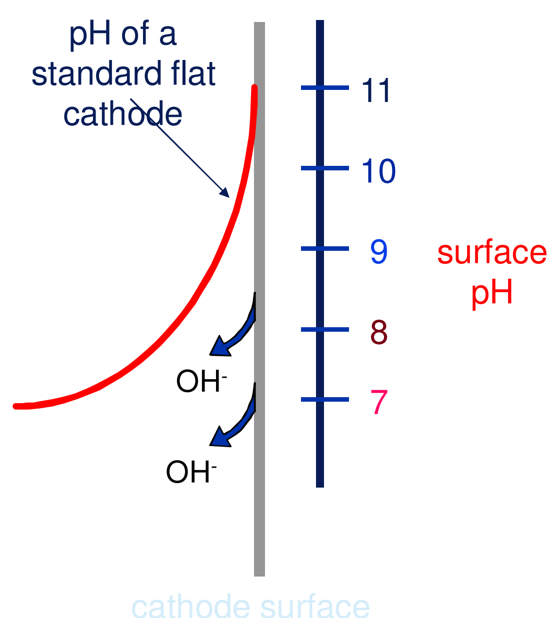
↓

High Local Surface pH

↓

High Scaling Potential

SOFTENER NEEDED in most locations



EDI Module : Scaling Risk

pH	Ca^{+2} (ppm)	HCO_3^- (ppm)
7	3600	10
8	360	10
9	36	10
10	3.6	10
11	0.36	10
12	0.036	10

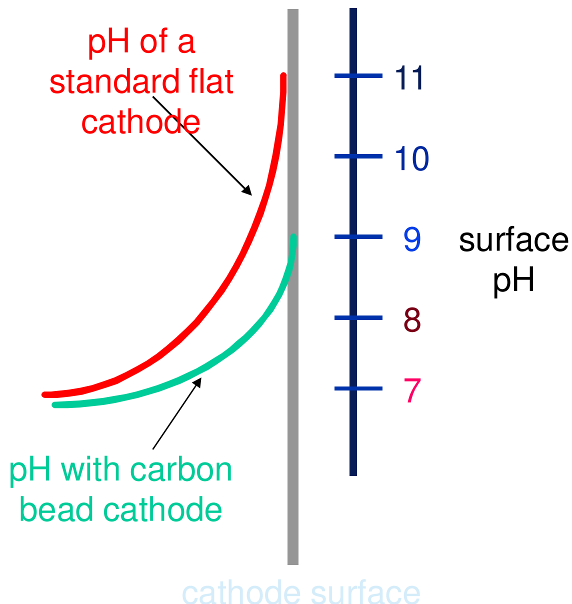
Carbon Beads: less steep pH gradient

High surface area cathode = generation of hydroxyls in a larger volume.

Reduces Local Surface pH

Reduces Scaling Potential

NO SOFTENER NEEDED



ElectroDeIonisation (EDI) Module

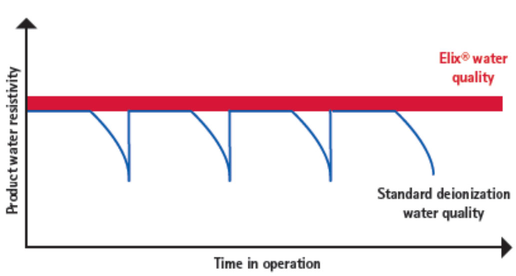
High Tolerance to Calcium
No softener required

New and Clean Design
Improved Performance

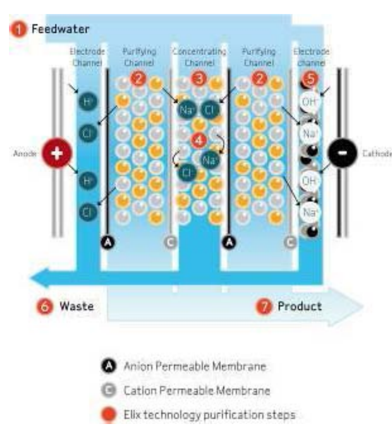
Compact Module
Compact System

Constant-quality, reliable Type II pure water

Electrodeonisation is the key to offering superior and consistant type II water quality, as with our other Elix systems and MQ Integral



The graph shows the superiority of Elix® technology over systems using ion-exchange resin packs. Resistivity drops dramatically when packs are exhausted.



ElectroDeIonisation (EDI)

Benefit

Very efficient removal of ions and small MW charged organic (R> 5 MΩ.cm)

Low energy consumption

High water recovery

Low operating cost

Low maintenance

No particulates or organic contamination (smooth, continuous regeneration by weak electric current)

Moderate investment

Limitations

Good quality (RO) feed water required
→ prevention of plugging (particles), fouling (organics, colloids) of ion-exchange resin and scaling at cathode

CO_2 not totally removed if at high level in feed water

UltraFiltration

Pyrogard 5000 inside

Milli Q Bicel/Synthesis

BioPak™

- Removal thanks to a membrane and pressure of organic molecules which size (molecular weight) is greater than the pore size.
- Typical LW usage :removal of pyrogens & Rnases by Milli Q with BioPak as final filter

Ultrafiltration – Definition

Ultrafilters = polymeric, asymmetric membranes, sometimes composite.

Very thin active layer (1µm)

Under pressure:

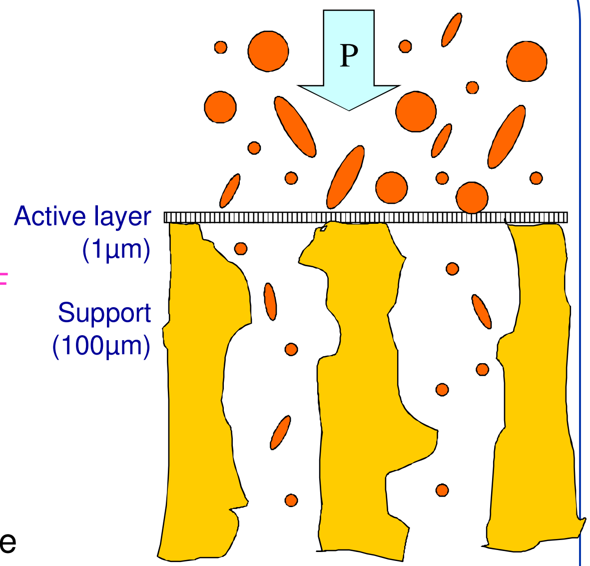
Molecules* with Molecular Weight greater then Nominal MW Limit *(NMWL)* of the UF

→ Rejection > 99 %

** MW > 1KDa*

Filter efficiency:

- expressed as Log Reduction Value *(LRV)*: logarithm of this rejection



Ultrafiltration

Benefits

Effective removal: >99% of molecules with MW > NMWL. Very efficient against pyrogens, nucleases, viruses, particulates.

No scaling risk (salts go through). Limited risk of fouling (fed w/treated water.

Low water waste (no reject).

Low maintenance.

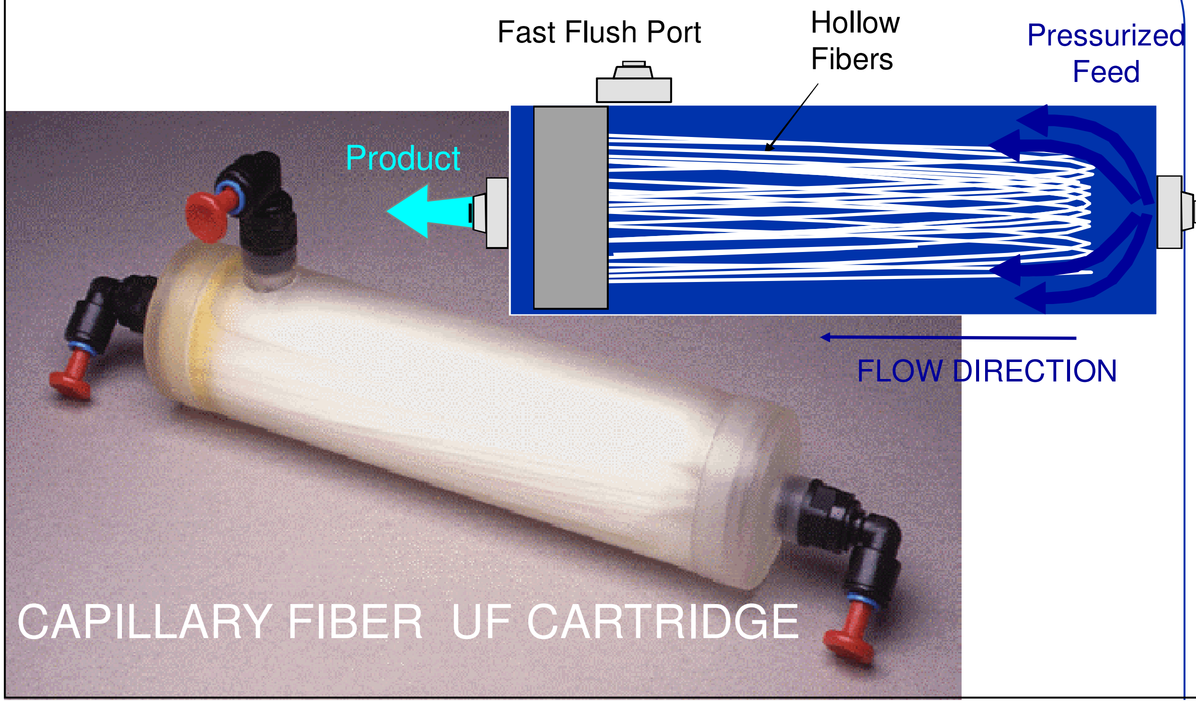
Limitations

Almost no rejection of ions, gases and low molecular weight organics.

Small organics not retained Cut-off of tightest UF membranes = 1,000 Da.

Pressure Need

LW old internal UF - Pyrogard 5000



UF Cartridge Maintenance

Pyrogard 5000

Automatic and regular flush

to prevent organic contaminants and colloids build-up on the UF membrane surface (0.5 min every 3 hours).

Sanitization by chlorine pills in Compact Milli-Q PF only

to prevent bacteriological development.

Sanitization and pyrogens destruction by NaOH

of the Milli-Q Biocel & Synthesis UF (cartridge and housing compatible with NaOH at high concentration)

BioPak

No maintenance !

LW Ultrafilter - BioPak

Point of use UF cartridge for ultrapure water systems.

Easy and cheap upgrades for systems without UF (Milli-Qs, Simplicity & Synergy, Direct Qs).

No flow rate loss

Sanitized by β radiation → no preservative

No need for sanitization → disposable !

Active Life Time: 90 days continuous operation

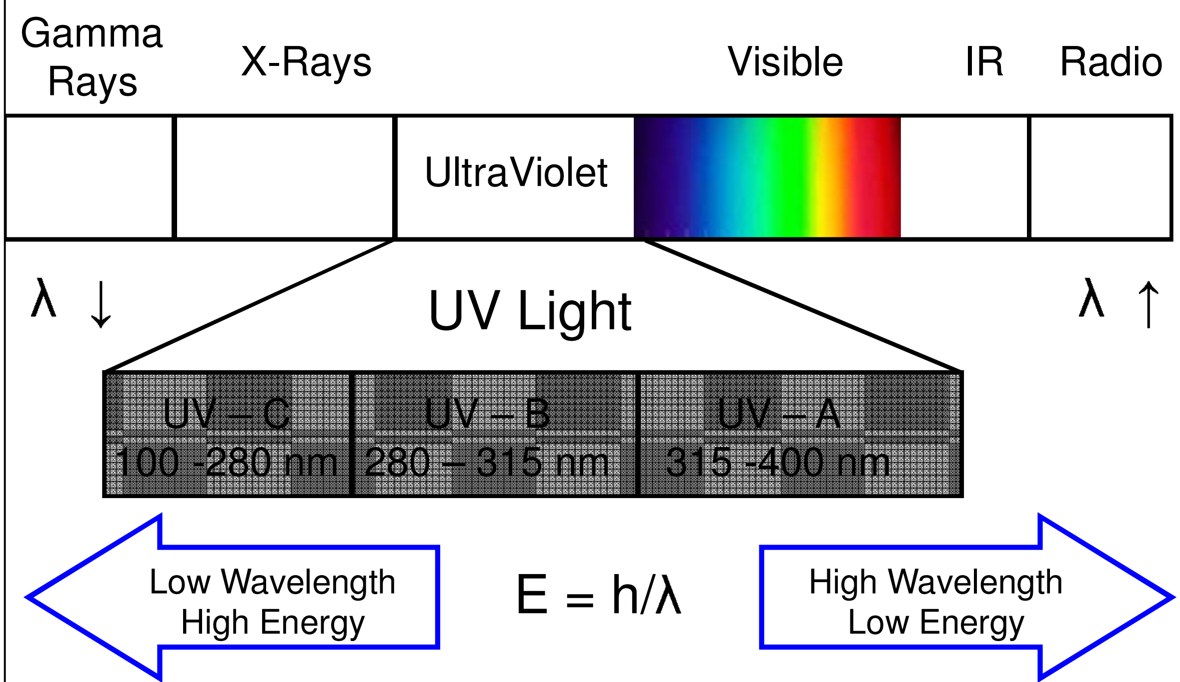
Bacteria Removal (<1 cfu / mL)

BioPak

UV Irradiation

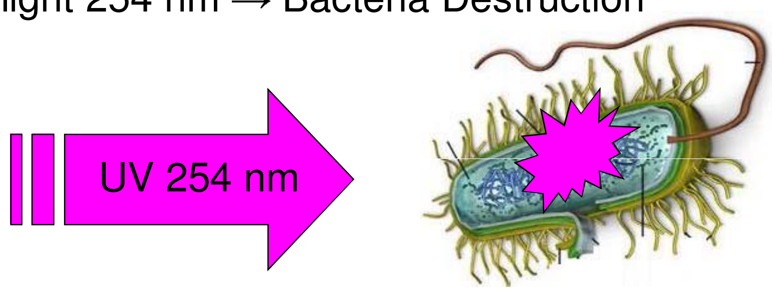
The Purification Technology for Bacteria & Organic Compounds

UV Light



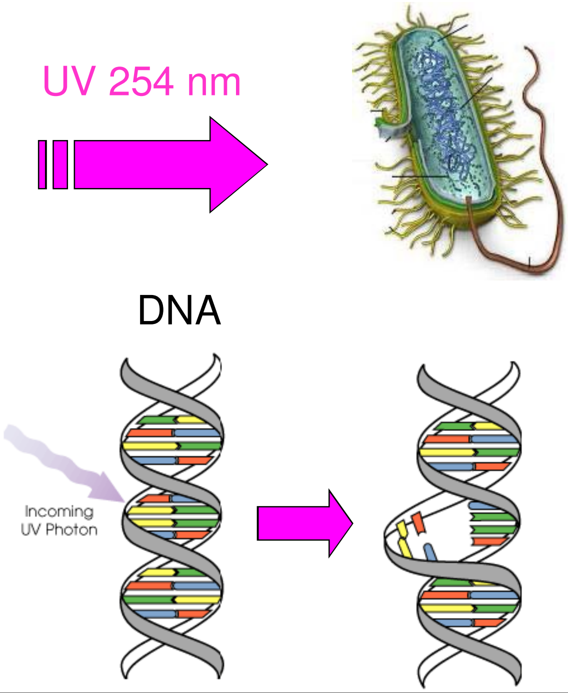
Usages of UV light in Lab Water Systems

UV light 254 nm → Bacteria Destruction



UV light 185 nm (actually 185 + 254 nm)
→ Oxidation of organic

UV Light 254 nm: Bacteria Destruction



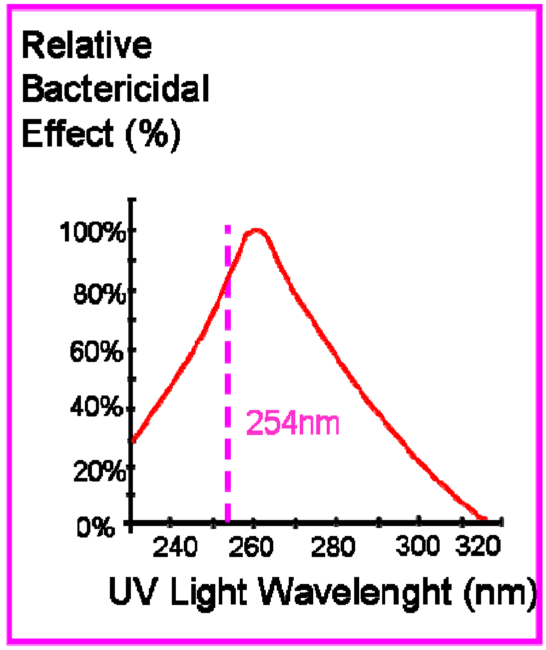


Photo-Oxidation of Organics (185 + 254 nm)

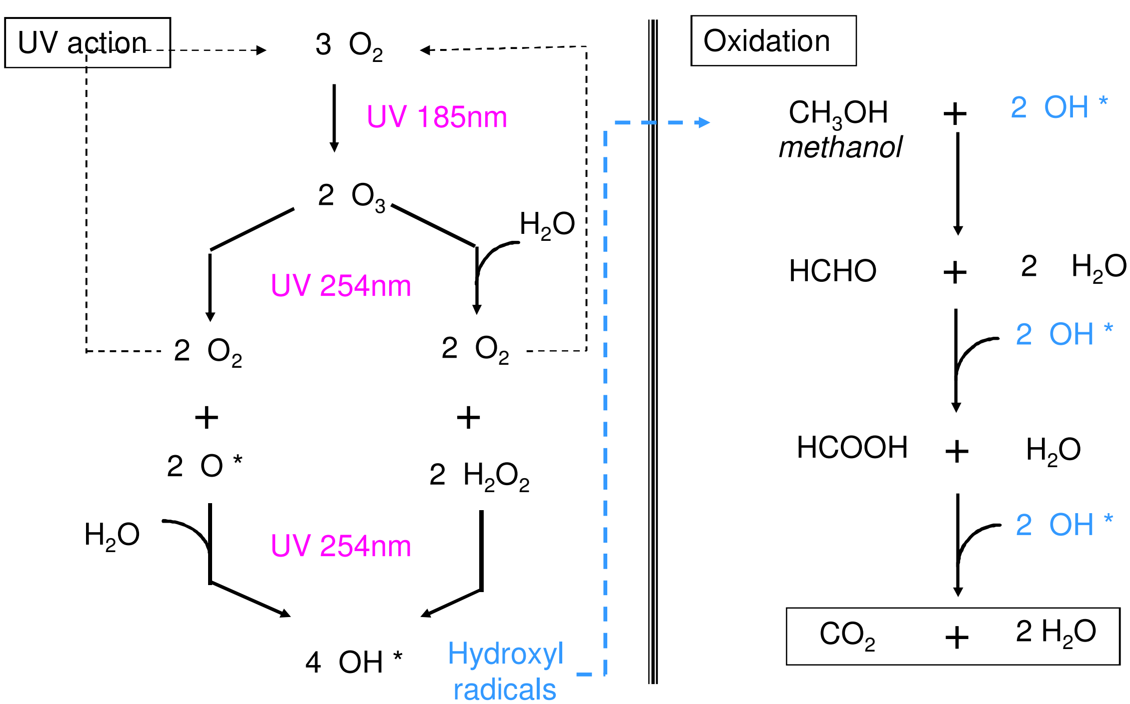


Photo-Oxidation of Organic Contaminants

UV energy catalyzes production of **hydroxyl radicals** (OH*).

These hydroxyl radicals generate reactions which **oxidize organic** compounds.

As the oxidation of organics progresses, reaction products become **more polar** (charges appear).

Ultimately all **organic** compounds are turned into $\mathbf{CO_2 + H_2O}$

The A10 cell measures the **change in conductivity** caused by CO_2 formed.

UV Technology (185 + 254 nm)

Benefits

- ❖Conversion of traces of organic contaminants to charged species and ultimately CO2 (185 + 254)
- ❖Limited destruction of micro-organisms and viruses (254)
- ❖Limited energy use
- ❖Easy to operate

Limitations

- ❖Polishing technique only: may be overwhelmed if organics concentration in feed water is too high
- ❖ Organics are converted, not removed.
- ❖Limited effect on other contaminants
- ❖Good design required for optimum performance.

Are All UV Lamps Equal ?

NO ! Many things can make the difference…

Quality of the ignition ballast will make the lamp last more or less – Millipore lamps last 4 x longer than others…

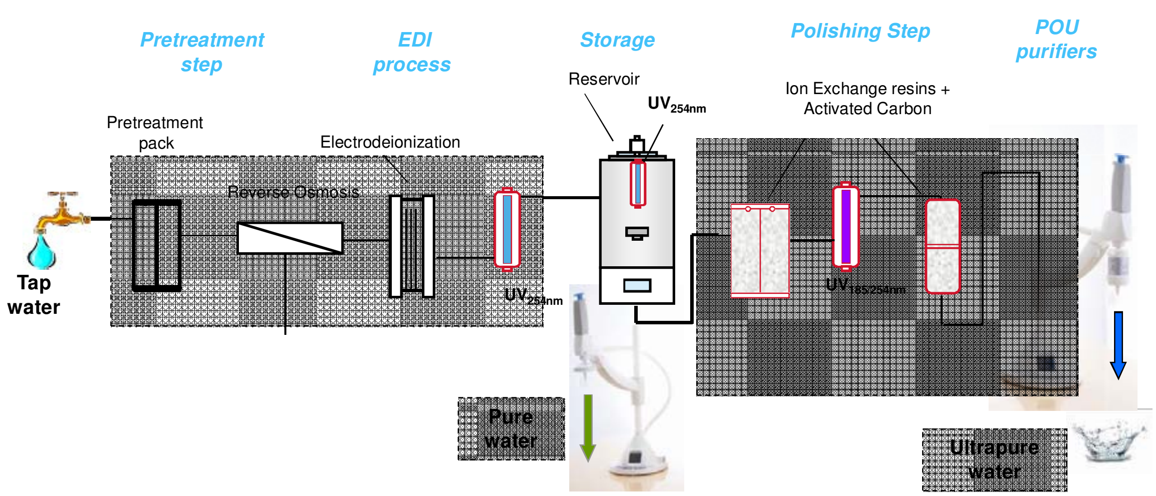
Quality of the Quartz will allow more or less light to go through.

→ Quartz with impurities allows only 254 nm light to go through

→ Quartz of high purity allows both 185 & 254 nm light to go through – Such a lamp is named in short a 185 nm lamp.

Lab Water purification systems :

An optimized assembly of water **purification** & **built-in monitoring** technologies to address our customers needs.



Contaminant Removal Efficiency

	Inorganics	Organics	Bacteria	Particulates
Carbon		●		◗
Microporus Filtration			●	●
Distillation	◕	◗	◕	◕
Reverse Osmosis	◕	◕	◕	◕
Ultrapure Ion Exchange	●	◗	◔	
Electrodeionization	●	◗	◗	
Ultraviolet Light		◕	●	
Ultrafiltration		◗	◕	◗

Common purification technologies and their effectiveness in removing major contaminants.

Laboratory Grade Water Norms

Different labotarory water grades have been defined by different regulatory bodies: ASTM, ISO, USP, NCCLS, CAP…

The grades correspond to both applications & specifications

Their role is both technical & economical

- Technical: select the adequate water quality for a specific applications
- Economical: avoid selecting a quality that is too high for an application as the cost of laboratory grade water production increases with the water quality

ASTM* Standards

	Electrical Conductivity µS/cm at 298 K (25 °C)	Electrical Resistivity MΩ-cm at 298 K (25 °C)	pH at 298 K (25 °C)	Total Organic Carbon (TOC), max, µg/L	Sodium, max, µg/L	Chlorides, max, µg/L	Total silica, max, µg/L	Maximum heterotrophic bacteria count, ml	Endotoxin, EU/mL
Type I	**0.0555**	**18**	**N. A.**	**50**	**1**	**1**	**3**	**-**	**-**
Type IA	0.0555	18	N. A.	50	1	1	3	10/1000	< 0.03
Type IB	0.0555	18	N. A.	50	1	1	3	10/100	0.25
Type IC	0.0555	18	N. A.	50	1	1	3	100/10	N. A.
Type II	**1.0**	**1.0**	**N. A.**	**50**	**5**	**5**	**3**	-	-
Type IIA	1.0	1.0	N. A.	50	5	5	3	10/1000	< 0.03
Type IIB	1.0	1.0	N. A.	50	5	5	3	10/100	0.25
Type IIC	1.0	1.0	N. A.	50	5	5	3	100/10	N. A.
Type III	**0.25**	**4.0**	**N. A.**	**200**	**10**	**10**	**500**	**-**	**-**
Type IIIA	0.25	4.0	N. A.	200	10	10	500	10/1000	< 0.03
Type IIIB	0.25	4.0	N. A.	200	10	10	500	10/100	0.25
Type IIIC	0.25	4.0	N. A.	200	10	10	500	100/10	N. A.
Type IV	**5.0**	**0.2**	**5.0 to 8.0**	**No limit**	**50**	**50**	**No limit**	**-**	**-**
Type IVA	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	10/1000	< 0.03
Type IVB	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	10/100	0.25
Type IVC	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	100/10	N. A.

*ASTM (American Society for Testing and Materials)

ISO® (International Organization for Standardization) - Several industry sectors

ISO 3696 standard

Parameter	Grade 1	Grade 2	Grade 3
pH @ 25 °C	Not applicable	Not applicable	5.0 – 7.5
Conductivity (µS/cm) @ 25 °C, max	0.1	1.0	5.0
Oxidizable substances, Oxygen (O) level (mg/l), max	Not applicable / Specific test to perform	0.08	0.4
254 nm absorbance (1 cm path), (AU), max	0.001	0.01	Not specified
Dry residue (mg/kg) after evaporation at 110 °C	Not applicable / Specific test to perform	1	2
Silica (SiO_2), (mg/l), max	0.01	0.02	Not specified

USP (United States Pharmacopoeia) - Pharmaceutical Sector
EP (European Pharmacopoeia) - Pharmaceutical Sector

Summary specifications	USP Purified Water	EP Purified Water	EP Highly Purified Water
Source water	Drinkable water according to EPA, EU		
Conductivity	< 1.3 µS/cm @ 25 °C*	< 4.3 µS/cm @ 20 °C	< 1.1 µS/cm @ 20 °C
TOC (ppb of C)	500 **	500 **	500 **
Bacteria Action level, max	FDA specifications: < 100 cfu/mL	< 100 cfu/mL	< 10 cfu/ 100 mL
Pyrogens (EU/mL)	NA	NA For dialysis < 0.25	< 0.25

* Refer to USP 32 <645> or EP Monographies

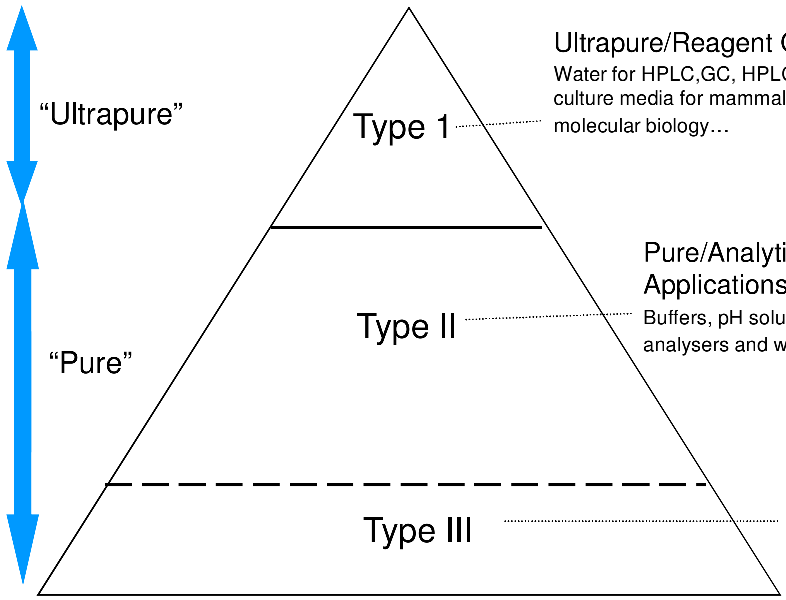
** Refer to USP 32 <643> or EP Monographies

Millipore LW Proposed Specifications

Water Quality Specifications (*Millipore guidelines*)

Contaminants	Parameter (units)	Type I	Type II	Type III
Ions	Resistivity (MΩ·cm)	> 18.0	> 1.0	> 0.05
Organics	TOC (ppb) Pyrogens (EU/mL)	< 10 < 0.001	< 50 NA	< 200 NA
Particulates	Particulates > 0.2 µm (units/mL)	< 1	NA	NA
Colloids	Silica (ppb)	< 10	< 100	< 1000
Bacteria	Bacteria (cfu/mL)	< 1	< 100	< 1000

Standards and Common Terms



Ultrapure/Reagent GradeCritical Applications
Water for HPLC,GC, HPLC ,AA , ICP-MS, for buffers and culture media for mammalian cell culture & IVF, reagents for molecular biology…

Pure/Analytical Grade Standard Applications
Buffers, pH solutions,culture media preparation ,clinical analysers and weatherometers feed.

Pure/Laboratory Grade General Applications
Glassware rinsing, heating baths, humidifiers and autoclaves filling

Applications (Alphabetical Order)	RiOs systems	Elix systems	AFS systems	Milli-Q systems
Analytical chemistry				✓
Atomic Absorption				✓
Autoclave (steam)	✓	✓		
Biochemistry automates		✓	✓	
Blank preparation				✓
Cell Culture				✓
Cellular biology				✓
Clinical analyzers		✓	✓	
Dilution of samples				✓
Dissolution testing		✓		
Electrophoresis				✓
Fog generation		✓		
Gas Chromatography				✓
General laboratory applications	✓	✓		
Glassware rinsing	✓	✓		
Heating baths	✓			
HPLC				✓
Humidity chambers	✓	✓		
Ice machine	✓	✓		
ICP-MS				✓
Ion Chromatography				✓
Microbiological culture media		✓		
Molecular biology				✓
Rinsing: wafers				✓
Stability chambers		✓		
Washing machines	✓	✓		
Weatherometers		✓		

Thank you for your attention !