Technical Brief

LABORATORY ULTRAPURE WATER

MILLIPORE

Selection and Control of Purification Media: The key to ultrapure water production in the laboratory

Summary

Although system design is clearly an important parameter in the production of ultrapure water, the final quality of product water ultimately depends on the quality of the purification media used in the system.

Purification media generally remove one or more classes of water contaminants. Their quality can be measured by their ability to remove the targeted contaminant(s), but also on their ability to avoid re-contaminating the purified water with extractable substances, and on the reproducibility of their performance over time.

Reproducible performance can only be ensured by careful selection of the purification media during the R&D/product development phase, and by stringent quality control on raw material, process control, and finished product during manufacturing.

Ultrapure water quality is routinely monitored via resistivity measurement, however, this parameter only measures the ionic contamination level and offers no information regarding other contaminants, such as micro-organisms, particles, and perhaps more importantly, organic substances.

The evaluation of overall product water quality from a system incorporating only resistivity measurement thus becomes largely a matter of faith in a given supplier who guarantees that the necessary Quality Control tests have been carried out on the purification media and materials used in the purification expendable(s).

In this case stringent quality control backed up by lot certification is the user's ultimate guarantee of performance.

In a recent technical advance, Millipore has introduced the Milli-Q® A10 Water System range, which combines organic purity monitoring, via Total Organic Carbon (TOC) measurements, along with the traditional ionic purity measurement via resistivity.

This technical brief describes three widely used purification media, and the key quality control tests employed by Millipore to ensure effective reproducible production of ultrapure water from the Milli-Q and Super-Q™ Ultrapure Water systems.

Purification Media

1 Activated carbon

is widely used to purify water. Its primary function in ultrapure systems is to remove organic contaminants by adsorption. There are two broad classes of activated carbon available, **natural and synthetic,** and their characteristics vary significantly depending on the starting material, manufacturing process, and supplier.

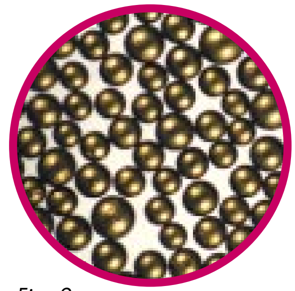
The most common starting material for **Natural Activated Carbon** is wood or coconut shell. This materials exhibits slow adsorption kinetics for low molecular weight organics, and releases ionic contaminants into the product water. For these reasons, this class of material is not used in Millipore Ultrapure Water systems, but is restricted to use as a low cost, efficient pretreatment prior to Reverse Osmosis.

Natural Activated Carbons

- Origin: Wood or coconut shell
- Pore size: 200 - 2000 Å
- Surface area: 1100 m^2/g
- Slow adsorption kinetics for low molecular weight organics
- Permanent release of mineral ions

Millipore use: RO protection (ROPAK™)

Fig. 1



Synthetic Activated Carbons

- Origin: pyrolysis of styrene beads
- Small pore size and relatively homogeneous: < 150 Å
- Surface area: 1100 m^2/g
- Rapid adsorption kinetics for low molecular weight organics
- Very low release of mineral ions

Millipore use: Milli-Q+ (QPAK, Organex™)

Fig. 2

Synthetic Activated Carbon is produced by the controlled pyrolysis of styrene beads. It has the same high porosity and surface area as natural activated carbon, but exhibits a rapid adsorption of low molecular weight organics, and a significantly reduced level of ionic extractables, as seen in Figure 3.

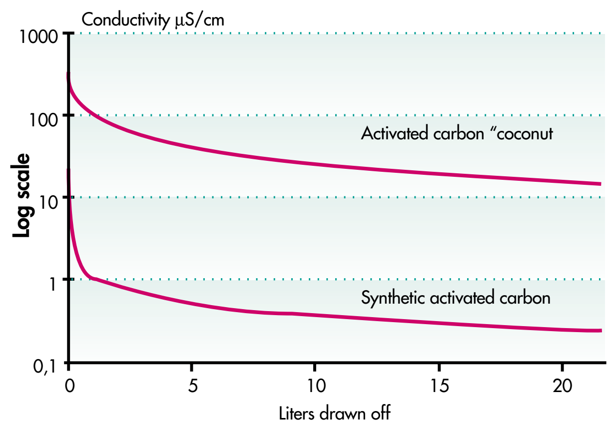


Fig. 3
Rinsing of Activated Carbon with Ultrapure Water

2 Ion Exchange Resin

retains ions by electrostatic forces. Resin production is a two-step process. A polymer matrix is created by the copolymerization of styrene and divinylbenzene (DVB). The percentage of DVB, which acts as a cross-linking agent between polystyrene chains, directly influences resin porosity, mechanical and chemical resistance, active site accessibility and, ultimately, the level of organic substances extracted in water.

The resin is then "activated" by the covalent binding of ion-exchange groups on the benzene ring of the styrene chains. The resin ion-exchange capacity, expressed in grams of NaCl, is largely determined at this step.

The different resins used by water system suppliers may thus have sharply different characteristics with regard to lot-to-lot consistency, resin bead size, porosity, chemical/mechanical resistance and degree of cross-linking. All of those characteristics influence the total binding capacity, speed and selectivity of ion-exchange, and the level of ionic, organic, and particulate extractables from the resin beads.

Model Structure of Ion Exchange Resin

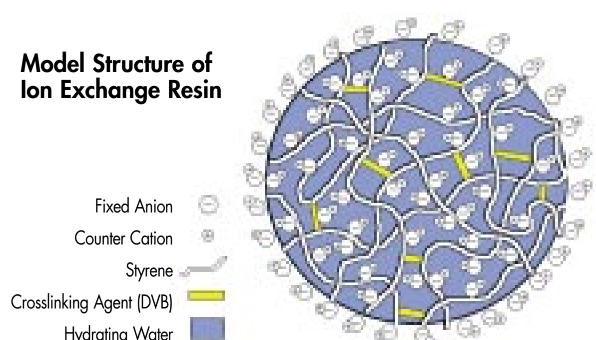


Fig. 4

3 Filtration Membranes

retain on their surface by a sieving mechanism 100% of the particles and bacteria larger than the membrane pore size. They should not be confused with ultrafilters, which remove large molecules, such as pyrogen and nucleases by size exclusion effects.

The quality of membrane filter materials is of particular importance because of their large surface area, and the fact that they are usually positioned very close to the point of dispense, where there are no subsequent steps to remove contaminants extracted from the filter device.

Point of Dispense Filter.
The Millipak® Disposable Filter Unit used at the point of dispense on the Milli-Q Ultrapure Water System is a pharmaceutical-grade filter device with an absolute 0.22 µm membrane for bacterial and particle retention. Figure 5 shows the low level of ionic and organic extractables from a Millipak when flushed with ultrapure water (18.2 MΩ-cm and 5 ppb TOC). Minimal extractables are shown by the rapid rinse back up to original feed water quality. The results obtained with another microfiltration membrane device are shown for comparison.

Rinsing of Filters for Ultrapure Water

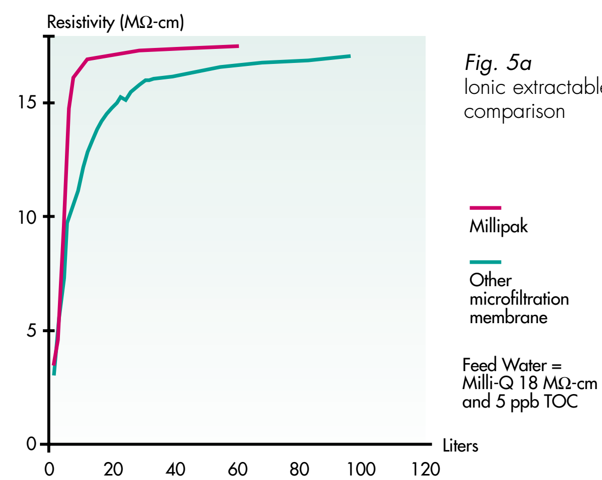


Fig. 5a
Ionic extractables comparison

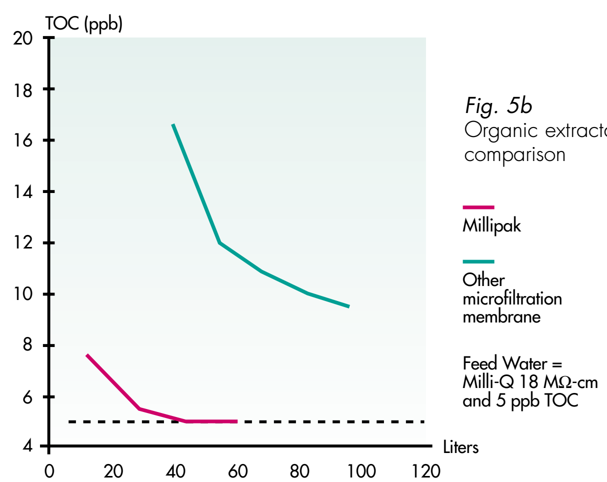


Fig. 5b
Organic extractables comparison

Ultrafiltration Membranes for Pyrogen-Free Water.
Pyrogen contamination of ultrapure water can affect a number of cellular, molecular, and clinical analyses: The hollow fiber ultrafiltration cartridge developed for the Milli-Q was extensively tested to quantify its ability to reduce endotoxin levels in ultrapure water (LRV > 4). Materials of construction were selected to minimize ionic and organic extractables, and to allow cartridge sanitization with concentrated NaOH. Two further Technical Briefs detail the measurement of pyrogens (TB064) and the design, testing, and maintenance of this hollow fiber device (TB065).

QPAK™ Certificate of Quality

Each lot of Millipore QPAK Purification Packs is sampled, tested and released to stock only when the following criteria are met:

- **Resistivity.** Achieves 18.2 MΩ-cm at 25° C.
- **Total Organic Carbon (TOC) Extractables.** Organics less than 10 ppb TOC after rinsing with reverse osmosis-purified water.
- **Ion Exchange Capacity.** Reached the minimum values of salt retention to a 10 MΩ-cm endpoint:

QPAK 1	75g NaCl
QPAK 2	45g NaCl
QPAK 3	50g NaCl

They are also tested for burst strength and integrity. **This certificate of quality is your guarantee of the purification media's performance according to Millipore's specification.**

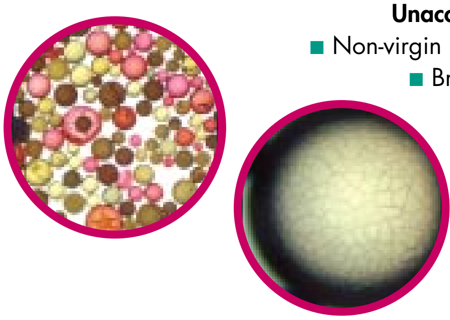
Certificate of Quality

Ion Exchange Resin Quality Control

Millipore's quality control process focuses on three main tests
A. Visual Inspection – Resin homogeneity and bead integrity
B. Salt Challenge – Ion-exchange capacity and exchange rate
C. Extractable Test – Organic extractable level and rinse rate.

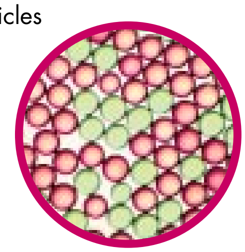
A Visual Inspection

Ion-exchange resin beads are colored by pH indicators and submitted to microscopic examination to determine the ratio of anionic/cationic resin, the bead size distribution, the degree of activation, and the absence of cracked or broken resin beads.



Unacceptable Ion-Exchange Resin
- Non-virgin resin (multiple regeneration)
- Broken resin beads (particles)
- Low degree of activation
- Resin bead cracked (production and/or regeneration problem)
- Particle generation imminent

- Homogenous: Size and Color
- No cracked resin beads or particles
- **High exchange capacity, low organic extractables and long operating life can be expected from this resin**



B Salt Challenge – Ion Exchange Capacity

A sample of ion-exchange resin is loaded on the test bench and fed with a controlled source of feedwater (Figure 6). Resistivity is monitored before and after the ion-exchange resin.

The resin's ability to rapidly reach 18.2 MΩ-cm is measured, at which point salt injection upstream of the resin begins, to provide a challenging feedwater with conductivity ~100 µS/cm. This salt challenge tests the resin's ability to strongly retain ions without ionic leakage.

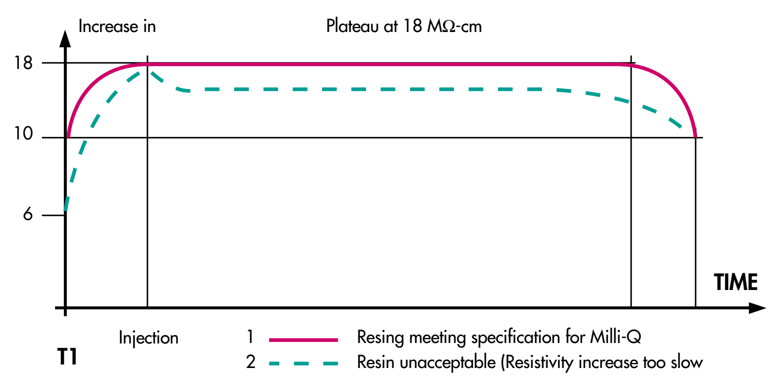


Fig. 7
Milli-Q Resin Capacity and Exchange Rate Test

Product water resistivity is monitored over time, to a 10 MΩ-cm endpoint. The resulting curve shows ion-exchange kinetics, and the amount of injected NaCl gives a direct measure of ion-exchange capacity. Figure 7 shows two profiles, one resin meeting Millipore specifications (full line), the other unacceptable (dotted line) due to ionic leakage, and slow ion-exchange kinetics.

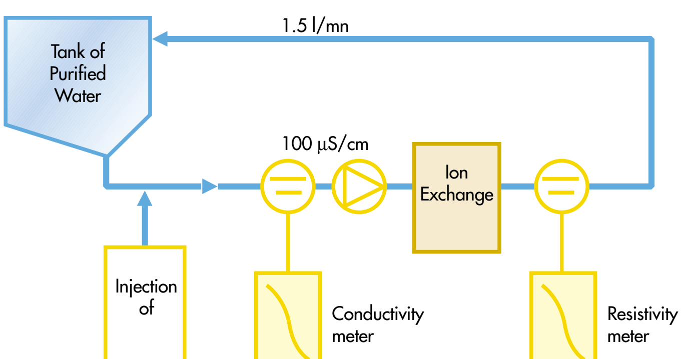


Fig. 6
Milli-Q Ion-Exchange Resin Quality Control Test of Capacity and Kinetics

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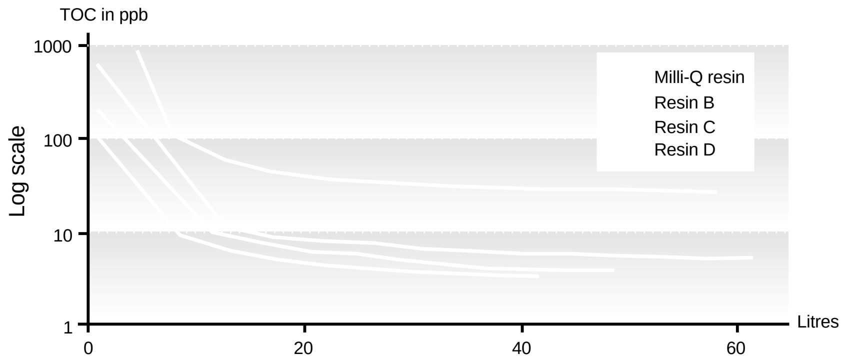

Fig. 8
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How to Maintain Ultrapure Water Quality

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(1) Division of Neurochemistry, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan
(2) Laboratory Water Division, Nihon Millipore Ltd, Tokyo, Japan
(3) Laboratory Water Division, Millipore S.A., St Quentin, France

For Additional Information

In the U.S. and Canada, dial **1-800-MILLIPORE (1-800-645-5476).** Outside of the U.S., contact the nearest office as listed below. Millipore Lab Water on the Internet: **http://www.millipore.com/H2O**

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U.S.A.
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Fax (617) 275-5550

In all OTHER COUNTRIES
Millipore Intertech (U.S.A.)
Tel. +1 (617) 533-8622
Fax +1 (617) 533-8630

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