cytiva

Maintenance of Biacore™ SPR systems

Biacore™ surface plasmon resonance (SPR) system is used to generate high-quality, information-rich affinity, kinetics, concentration, specificity, and comparability data in real-time. For continuous high performance, regular maintenance and cleaning of the system is advised. Biacore system arrives with built-in tools for cleaning and maintenance that users can perform. Other procedures are completed by a Cytiva representative during routine service visits. This application guide describes how to perform routine cleaning and maintenance on your Biacore system, what tools are available, and how frequently you should run them. The guidelines are applicable for Biacore 1 series, Biacore 8 series instruments and for most parts of Biacore T200, Biacore S200, and Biacore X100 instruments.

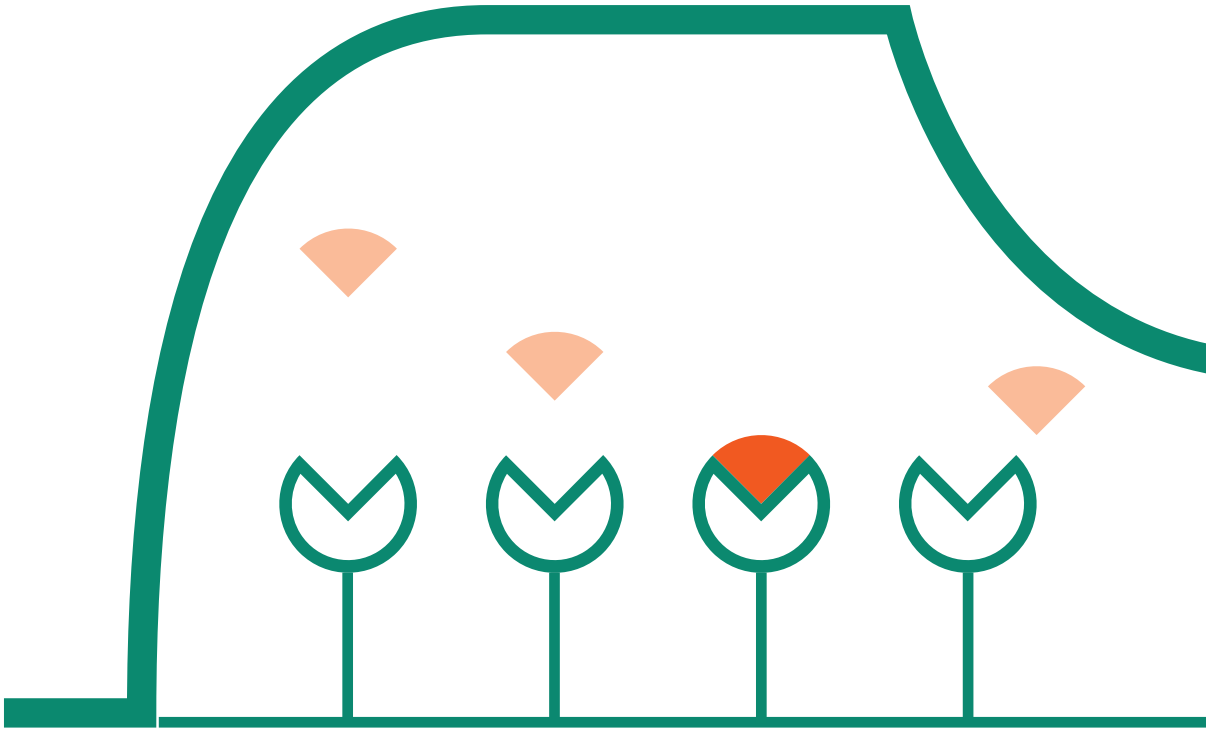

Table 1. Terminology

Term	Meaning
Desorb	Cleaning procedure involving washing with two solutions: Desorb 1, 0.5 % sodium dodecyl sulphate (SDS) and Desorb 2, 50 mM glycine pH 9.5. Both solutions are passed over the sensor surface during the procedure.
Desorb and sanitize	More extensive cleaning which involves washing with Desorb 1 and Desorb 2 followed by disinfection with 0.6-1.0 % sodium hypochlorite solution. Used to remove microorganisms from crude samples such as plasma. All solutions are passed over the sensor surface during the procedure.
Shutdown	Procedure for proper shut down of Biacore system. Includes wash of IFC and flow system with water and 20% ethanol followed by an injection of air to remove fluid from IFC and flow system.
Normalize	Procedure that adjusts detector response to compensate for small variations in the optical system. These arise when sensor chips are docked and undocked.
System check	Procedure that performs a series of tests to check that the system performs properly. System check is typically run to check instrument performance, for troubleshooting, or in preparation of a service visit.
Standby flow	Standby flow maintains a continuous low flow of liquid through the flow system and over the sensor surface. The purpose of Standby flow is to maintain a buffer flow through the flow system to keep ligands on the sensor surface active and to keep the flow system from drying out.
Series S Maintenance Chip Sensor Chip Maintenance	Sensor chip with a glass surface instead of gold. Recommended for use during maintenance of Biacore systems.

Tips and tricks

- If you don't intend to continue using the sensor chip currently docked in your instrument there is no need to replace it with a maintenance chip before running maintenance tools using harsh solutions.
- Use the ***Activity queue*** to queue a ***Desorb*** procedure directly after your regular assays.
- If you queue the ***Desorb*** procedure to run after your regular assays, make sure that the sample compartment temperature is higher than 15°C as SDS precipitates at temperatures lower than 10°C.
- Do not use sodium hypochlorite products for ***Sanitize*** longer than 12 months after the quality control date to make sure that the chlorine concentration is sufficient for disinfection. Active chlorine concentration decreases with time. The quality control date is typically stated in the Certificate of Analysis for the product.
- Make sure that the running buffer in your system is compatible with Desorb 1 solution (0.5 % SDS). Do not use running buffer with additives containing metal ions as SDS precipitates with common metal ions such as potassium and magnesium.
- Do not use plain water as running buffer after ***Desorb and Sanitize***. Water rinses sodium hypochlorite insufficiently compared to running buffer. Residues of sodium hypochlorite can damage sensor chips.
- Run ***System check*** with solutions specified in the tool and always on an unused Sensor Chip CM5 so procedure results are correct.
- The sensor chip used for ***System check*** is not affected by the procedure and can be used for subsequent assays.
- The ***Desorb*** procedure can be used to wash with solutions other than Desorb 1 and 2 solutions. Simply replace the regular solutions with the wash solutions of your choice.
- If you intend to wash with other solutions than what is recommended, check Operating instructions for your instrument to make sure that these solutions are not harmful to the flow system.

Maintenance of Biacore systems

Maintenance schedule

Table 2. Maintenance for Biacore systems is recommended with the following interval

Procedure	Interval
Desorb	Weekly
Desorb and sanitize	Monthly
Normalize	Run the tool periodically (about once a month) to test your system and fine-tune detector responses.
System check	Run the tool periodically (about once a month) to test your system or in preparation for a service visit.
Shutdown	Run this procedure if the instrument won't be used for more than seven days.

Sensor chip for maintenance procedures

Maintenance procedures available for Biacore system are designed to clean all parts of the flow system including the sensor surface. Some solutions used in these procedures are harsh and can be damaging to ligand coupled to the sensor surface. To avoid damage, undock any immobilized sensor chips that is intended for continued use prior to starting the procedure. Then dock a Series S Maintenance chip or Sensor Chip Maintenance, which have a plain glass surface instead of gold that can withstand harsh cleaning solutions. Maintenance chips can be reused for multiple rounds of maintenance.

If you don´t intend to use the docked sensor chip for more experiments, you can also keep that chip docked in the instrument and run your maintenance procedures. Maintenance can be run on previously used sensor chips.

Desorb

The Desorb procedure is run using two solutions, 0.5 % SDS (Desorb 1) and 50 mM glycine-NaOH pH 9.5 (Desorb 2). Run the ***Desorb*** procedure weekly to clean the flow system in your Biacore system. If the instrument has been run with sticky or crude samples, run ***Desorb*** before switching to other assays or sample types. The procedure is run with solutions pipetted into a microplate or in vials. Before inserting a microplate or vial containing Desorb 1 into the sample compartment of your instrument, make sure the temperature is set to 25°C to avoid precipitation of the SDS solution. After the procedure is finished, run a ***Prime*** or ***Change solutions*** procedure before docking a new sensor chip.

To start the Desorb procedure, navigate to the maintenance part of the software and follow the instructions.

Desorb and sanitize

The ***Desorb and sanitize*** procedure includes the ***Desorb*** procedure followed by a disinfection step using 0.6-1.0% sodium hypochlorite to prevent bacterial growth. Run this procedure once a month or after exposing the system to crude samples such as plasma. This procedure also cleans and disinfects the buffer lines of your Biacore system. All solutions are prepared in bottles. When running the procedure, place the tubes for buffer and water in the required bottle for each step according to the software instructions. Be careful when removing tubing from the disinfectant solution to avoid splashing.

After completion of the procedure, run running buffer in standby mode for three to four hours or overnight before docking a new sensor chip. If you intend to use Sensor Chip SA immediately after running the sanitize procedure, run ***Prime*** or ***Change solutions*** for all buffer inlets that you intend to use before docking Sensor Chip SA. Any sodium hypochlorite remnants in the system will damage this sensor chip.

Shutdown

The ***Shutdown*** procedure should be used when the instrument won't be used for more than seven days. This procedure washes the flow system with water followed by 20% ethanol. The system is then flushed with air, so the flow system is dry before the instrument is turned off. When ***Shutdown*** is completed, the sensor chip is undocked. Remove the sensor chip from your instrument and close the sensor chip port. Then turn off your instrument by pressing the power button on the back of the instrument. Biacore 8 series, Biacore T200 and Biacore S200 instruments require the clamps of the peristaltic pumps to be released after shutting down the instrument. Refer to the operating instructions of each instrument model for instructions on how this is done. This operation is not needed for Biacore 1 series instruments.

Note: For Biacore T200 and Biacore S200 systems, ***Shutdown*** is run using 70% ethanol.

System check

System check performs a comprehensive review to maintain proper system performance. System check can also be used as a troubleshooting tool or in preparation of a service or maintenance visit by a Cytiva representative. It is recommended to run System check once a month. The procedure tests the following system features:

- Liquid supply
- Injection quality
- •Mixing capability
- Refractometer status
- Noise level
- Buffer selector

The procedure requires an unused Series S Sensor Chip CM5, HBS-EP+ buffer and Biacore test solution (15% sucrose in HBS-EP+ buffer).

To run the procedure, navigate to the maintenance part of the software and open the tool. Prepare reagents and start the tool according to software instructions. The results of the System check are stored in the database (Biacore 1 series and Biacore 8 series) or on the hard drive of your system controller. Guidelines to interpret the results of a ***System check*** is provided in the operating instructions of your instrument.

Normalize

The ***Normalize*** tool adjusts detector response to compensate for small variations in the optical system that arise when sensor chips are docked and undocked. It is recommended to run the ***Normalize*** tool around once a month to test your system and fine-tune the detector responses. For best performance, run the tool after docking a new chip, either before a ligand is attached or before your first analysis run using the immobilized chip. ***Normalize*** is run using BIAnormalizing solution (70% glycerol).

Cleaning instrument exterior

When required, clean the exterior of the instrument with a soft cloth or tissue, moistened with water or a mild detergent. If necessary, clean the caps on the waste and liquid supply bottles as follows:

- Start by stopping ***Standby flow***
- Unscrew cap from the bottle.
- Remove tubes from cap.
- Rinse cap in warm water, dry and screw it back on the bottle
- Re-attach tubes to the cap.

Do not use strong acidic or basic solutions to clean the outside of your instrument.

Cleaning the sample hotel and sample compartment

To clean the sample hotel or sample compartment, remove all sample trays and wipe the surfaces with a moistened cloth or tissue. If cleaning is required in inaccessible places, contact your Cytiva service representative for assistance.

Clean spills in the sample compartment

When runs are performed below ambient temperature, condensation can occur in the sample compartment. Condensed water may run on to the drip tray underneath the instrument and normally evaporates. In humid atmospheres with a large temperature difference between ambient and sample compartment, remove and empty the drip tray when necessary. In the event of malfunction that causes buffer or reagent spills in the sample compartment (e.g., blockage in the connector block or leakage from a liquid supply tube), contact your Cytiva service representative.

Standby flow

Standby flow is a low flow rate, constant flow of liquid to keep the flow system and sensor surface hydrated. ***Standby flow*** should be run using running buffer and not water. Using running buffer instead of water increases the lifespan of the IFC. IFCs tend to get softer when in use but recover during ***Shutdown***. The tendency to soften is accelerated with the use of water and acidic coupling buffer. If the IFC becomes too soft, there is risk of the IFC valves becoming stuck, which results in IFC failure. By using HBS-EP+ or similar during ***Standby flow*** this risk is significantly reduced.

Cleaning before service

For protection and safety of service personnel, all equipment and work areas must be clean and free of any hazardous contaminants before a Service Engineer starts maintenance work. Run the ***Desorb and sanitize*** procedure and wipe the exterior of the instrument with a cloth or a tissue. Remove any used microplates and vials from the sample compartment. Empty the waste bottle. Leave the instrument on ***Standby flow***. Inform the service engineer if hazardous samples have been run in the instrument so they can take extra precaution.

Working with Biacore systems under biosafety conditions

Analysis of infectious and toxic material in Biacore systems requires special cleaning and maintenance considerations. Note, this section is only intended to highlight practices and working procedures for the instrument. Ultimately, the end user is responsible for safe analysis and disposal of biosafety material. Follow local laws and regulations.

- Run ***Desorb and sanitize*** according to system maintenance instructions. This procedure cleans all interior parts of the flow system that were in contact with the samples.
- Safely handle the contents of the waste bottle. One option is to add an appropriate disinfectant or deactivation solution to the waste container prior to performing experiments. Use a start concentration that results in an appropriate concentration for the full bottle. For example, weigh sodium hydroxide into the empty waste bottle and add a small amount of water. The final concentration of sodium hydroxide when the bottle is full should be approximately 200 mM. The waste is then considered safe and can be disposed of afterwards according to lab regulations.
- Adding Virkon to the waste is another solution to deactivate infectious material. At run start add Virkon to the waste bottle to an expected end concentration of 1%. At the end of the run add another 1% of Virkon to the waste vessel and let it sit for 30 min prior to disposal.
- All surfaces on the system that were in contact with infectious material should be cleaned with Virkon 1% or 70% ethanol. Let it rest for 15 min and then wipe clean with water. This includes rack trays, reagent racks and the autosampler compartment. For Biacore T200 and Biacore S200 instruments, make sure you do not touch the needle when cleaning the autosampler compartment.

- Dispose of used microplates and vials according to your lab regulations.
- If the system is in a BSL classified lab we recommend cleaning, then letting it dry for 1 week before moving it out of the lab.

These are general tips and considerations. Your team must adopt suitable procedures for cleaning depending on the type of infectious or toxic material used in your lab.

Additional procedures for cleaning your Biacore system

Cleaning after coupling of biotinylated ligands

Isopropanol 50% in 1M NaCl and 50 mM NaOH is an effective cleaning solution in several instances. For example, this solution is recommended to wash away remnants of biotin in the flow system after coupling biotinylated ligands on Sensor Chip SA and Sensor Chip NA. Mix equal parts of isopropanol and 2 M NaCl in 100 mM NaOH. Use the wash solution within a week.

Superclean

In rare occasions cleaning your Biacore systems using the ***Desorb and sanitize*** procedure is not sufficient. This applies especially to sticky and fatty samples such as milk. In situations like these, use the more extensive ***Superclean*** procedure. Superclean is available as a tool in the Biacore T200 and Biacore S200 software but not for Biacore 1 series and Biacore 8 series instruments. The procedure can be set up also in these instruments, either by using the ***Change all*** procedure for each step of the cleaning procedure or by using ***Activity queue*** to queue all steps of the procedure. There are two versions of the procedure, one for protein assays and one for small molecule assays.

Note: All solutions are passed over the sensor surface. Dock a Series S Maintenance chip before starting the procedure.

Note: Superclean should not be used for regular cleaning of your Biacore instrument. For regular cleaning refer to ***Desorb*** and ***Desorb and sanitize*** procedures.

Superclean using *Change all* procedure

Prepare reagents in separate bottles. Run a ***Change all*** for each step by placing all tubings in the respective bottle in the order described below.

Table 3.

Step #	Solution proteins	Solution small molecules
1	Deionized water at 50°C (max temp)	Deionized water at 50°C (max temp)
2	1% acetic acid	1% acetic acid
3	0.2 M sodium bicarbonate	0.2 M sodium bicarbonate
4	6 M guanidine-HCl	50% DMSO
5	10 mM HCl	10% DMSO

Superclean using the *Activity queue*

Pipette reagents in a microplate or in vials. Place all tubings in warm water (not more than 50°C). Add the following commands to the Activity queue and start the procedure:

Table 4.

Step #	Command proteins	Command LMW
1	Change solutions with water at 50°C (max temp)	Change solutions with water at 50°C (max temp)
2	Change solutions with water at 50°C (max temp)	Change solutions with water at 50°C (max temp)
3	Desorb with 1% acetic acid (both steps)	Desorb with 1% acetic acid (both steps)
4	Change solutions with water at 50°C (max temp)	Change solutions with water at 50°C (max temp)
5	Desorb with 0.2 M sodium bicarbonate (both steps)	Desorb with 0.2 M sodium bicarbonate (both steps)
6	Change solutions with water at 50°C (max temp)	Change solutions with water at 50°C (max temp)
7	Desorb with 6 M guanidine- HCl and 10 mM HCl	Desorb with 50% DMSO and 10% DMSO
8	Change solutions with water at 50°C (max temp)	Change solutions with water at 50°C (max temp)
9	Change solutions with water at 50°C (max temp)	Change solutions with water at 50°C (max temp)

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