Technical Note

Preventing damage to Nanopore Reader amplifiers: Best practice for flow cell handling

This user guide outlines the best practices for using flow cells in Nanopore Reader amplifiers, aimed at preventing damage caused by leakage or improper handling.

Important note: This guide does not explain how to operate the flow cell. Instead, it provides recommendations to help prevent damage to the amplifier resulting from improper use. Detailed instructions for conducting experiments with these flow cells can be found in the related guides referenced in the following sections.

Sections

1- **Flow Cell Handling and Best Practices**

   Provides guidance on the proper use of flow cells, including recommended handling procedures and preliminary tests to perform before inserting them into the amplifier.

2- **Amplifier Functional Checkout**

   A detailed procedure for functionally checking the amplifier to determine whether it has been damaged after exposure to electrolyte solution.

3- **Visual Examples of Electrolyte-Induced Damage to Electronics**

   Presents visual examples and explanations of the damage that occurs when electrolyte solution enters the amplifier.

1- Flowcell Handling and Best Practices

Elements amplifiers are advanced electronic instruments designed for ultra–low-noise measurements of extremely small ionic currents, ranging from a few hundred femtoamperes up to several hundred nanoamperes, depending on the specific model.

All experimental configurations rely on the use of fluidic devices, the **solid-state nanopore flowcells** or **BLMchip_MM**, which enable measurements on solid-state nanopores or artificial lipid membranes.

To achieve ultra–low-noise current measurements, the electrodes of each flow cell have been positioned very close to the amplifier's input contacts in order to reduce parasitic capacitances and allowing the system to reach its lowest possible noise levels.

As a consequence of this design requirement, the electrolyte solution used inside the flow cells is physically located only a short distance from the amplifier's electronic contacts.

⚠️ **Even minor spills or leaks may reach the electronics and cause permanent amplifier damage.**

To prevent damage, **strict care must be taken to avoid any contact between the electrolyte and the electronics**.

All Elements flow cells are individually tested to ensure that, when used correctly, no electrolyte leakage can reach the electronics. However, **incorrect handling, especially when adding or removing liquids, can lead to severe damage**, as described in later sections.

Below are the recommended good practices for using Elements two main flow cell types, the **BLMchip_MM** and **Nanopore Flowcells**, along with key precautions and tips to avoid damaging the amplifiers.

1. BLMchip_MM Flowcells

BLMchip_MM devices are designed for measuring ionic currents through biological nanopores (membrane proteins such as ion channels, bacterial toxins, etc.) reconstituted into artificial lipid bilayers.

These flow cells are shipped **fully assembled and ready to use** and **must not be disassembled or modified** in any way.

Each BLMchip_MM is individually tested to ensure that no liquid can leak through bonded parts. After every experiment:

- Clean the flow cell strictly following the dedicated user guide.
- **Do not** use solvents or cleaning methods other than those specified.

During electrolyte loading and bilayer formation (Montal–Mueller or bubble method):

- **Pipette slowly and carefully to avoid liquid spills.**

- Keep the cis and trans compartments within the recommended volumes (max 110 uL), as described in paragraph 3.2 of the same user guide.

- **Exceeding the indicated volumes may cause electrolyte to overflow**, potentially reaching the internal contacts of the amplifier and causing serious damage.

Periodic Leak Check

After several use/cleaning cycles (e.g., 5–6), verify that the flowcell still shows no signs of leakage:

1. Place the BLMchip_MM (mounted on its PCB) on blotting paper.
2. Add **100 µL** of electrolyte to each compartment.
3. Leave the BLMchip_MM on the absorbent paper for ~30 minutes.
4. Periodically check that the paper remains dry and that no liquid appears on the side walls.

2. Nanopore Flowcells (Solid-State Nanopores)

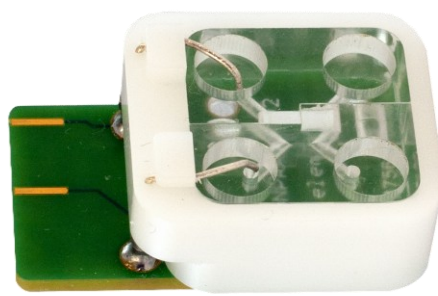
Nanopore flow cells require the **assembly of the nanopore chip before each experiment**. Prior to any operation, verify that the chip thickness matches the compatibility range of the flow cell model:

- **Nanopore Flowcell 4×4 & 5×5 PMMA – 1.0** → chip thickness **200–300 µm**

- **Nanopore Flowcell4×4 & 5×5 PMMA – 1.2** → chip thickness **400–500 µm**

- **Nanopore Flowcell4×4 & 5×5 PMMA – 1.4** → chip thickness **500–600 µm**

Using chips outside the specified thickness ranges can lead to leaks and severe damage to the amplifier’s electronics.



After each experiment:

- Clean the flowcell following the dedicated user guide.
- Inspect all PMMA parts and gaskets for cracks, deformation or any defect that might compromise sealing.

Leak check before inserting the flow cell into the amplifier

As described in the user guide (page 4), it is convenient to verify the proper flow cell sealing before inserting it into the amplifier:

- Assemble the nanopore chip into the flow cell, as described in the related user guide.
- Place the flow cell **on absorbent paper, outside the amplifier**.
- Fill both compartments with electrolyte.

- Check for leaks. Only once proper sealing is confirmed, gently insert the flowcell into the amplifier slot.

This procedure helps highlight fairly significant leaks in the flow cell. However, leaks may be very small and only become visible to the naked eye after some time. These minor leaks are easily noticeable during an experiment: if all of a sudden the current signal increases dramatically or even reaches saturation, it is likely that there is a leak in the flow cell. In that case, immediately remove the flow cell from the device and perform a functional checkout, as described in the following section, to verify that the amplifier is still in optimal condition.

Adding or Removing Solutions During the Experiment

Use a laboratory pipette with great care to avoid spills. Insert the pipette tip lightly into the dedicated fluidic channels (as described at pag 7 of the related user guide) without applying mechanical pressure. Pressure or force on the channels may cause small displacements of internal components and result in leakage.

Amplifier functional checkout procedure

If an electrolyte solution accidentally reaches the amplifier's input contacts, unwanted current will flow through unintended leakage paths. **This typically results in abnormal baseline behavior or, in the worst case, in the amplifier saturation even under open-circuit conditions.**

<u>If you suspect, or are certain, that electrolyte solution has reached the amplifier contacts, follow the procedure below.</u>

The described procedure refers to the eNPR 100kHz amplifier but the same operations can be made on the eNPR 10MHz amplifier, using the related control software, EMCR.

If liquid is visibly present on the amplifier's white slide (the flowcell insertion area), carefully dry it as thoroughly as possible using clean absorbent paper before proceeding.

1. Baseline Stability Test

1. Connect the amplifier to your PC and launch the **EDR4** software.
2. Ensure that **no model cell, flowcell, or BLMchip** is inserted in the amplifier. Close the lid.
3. Verify that the **Controls** widget settings match those shown in the left-hand panel of the reference figure. In the 10MHz device, just set the lower bandwidth (1MHz); the other options (voltage range, voltage command filter and current range) are not available.

4. **Ensure that the measured current signal is stable at 0 pA, with no noticeable drift.** If, at this stage, the current signal causes the amplifier to saturate, do not proceed to the next step. Please contact support@elements-ic.com, including a screenshot of the software interface showing the saturated signal, and specify that it was recorded while the amplifier was in open-circuit mode

2. Open Circuit Resistance Test

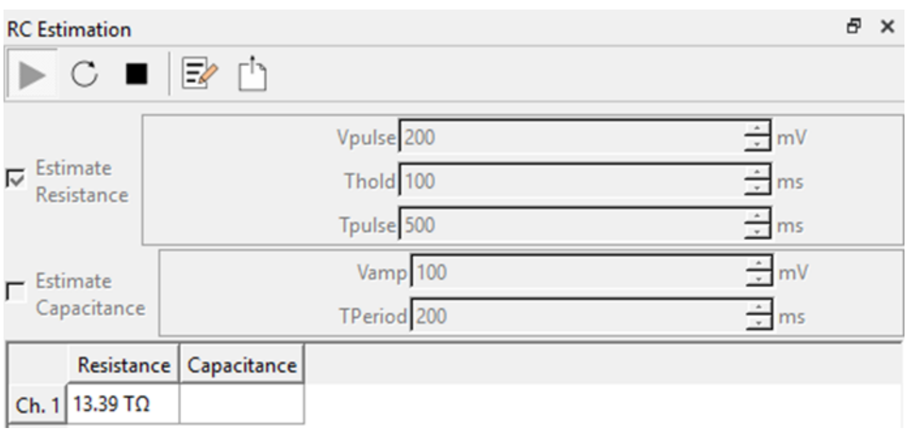
1. Open the **RC Estimation** widget.
2. Enable **Estimate Resistance** ☑.
3. Set the stimulus parameters exactly as shown in the reference screenshot.
4. Press **Play** (▶) to start the measurement.

A periodic square-wave voltage stimulus will be applied, and the estimated resistance will be displayed.

⚠ **The measured resistance must not be lower than 1 TΩ.**

If the value is lower, please contact support@elements-ic.com attaching a screenshot showing at least the RC estimation widget, the current and voltage traces and the control widget settings.

Press **Stop** before proceeding to the noise test.



For the 10MHz device, use the IV graph tool, available in EMCR software, to measure the resistance. This can be done, for example, by testing a few voltages (e.g. ±600 and ±200 mV) and fitting the data with a linear equation using the dedicated button. For more details on the IV graph tool, please see [this]() guide at page 4.

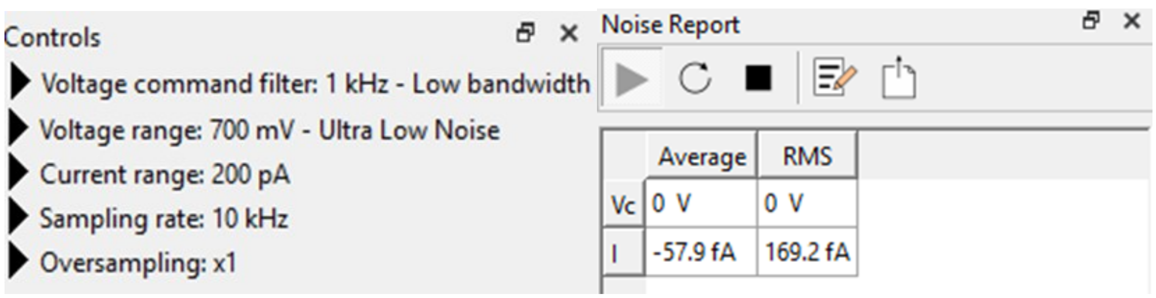
3. Noise Test

- Ensure that a constant **0 mV** bias is applied (verify in the oscilloscope window).
- Confirm that the **Controls** widget settings match those shown in the left-hand panel.
- Open the **Noise Report** tool (from the *Analysis* menu).

- Start the analysis by clicking the green **Play** button (▶).

⚠ **The RMS noise must not exceed 300 fA.**

If the noise is higher contact support@elements-ic.com attaching a screenshot showing at least the noise report result, the current and voltage traces and the control widget settings.

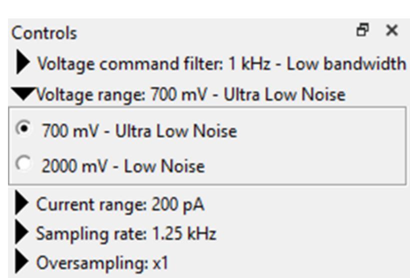


4. Model Cell Resistance Check

- Set the Model Cell to either **LN** or **ULN** mode and insert it into the eNPR 100 kHz amplifier. Close the lid.
- Connect the amplifier to your PC and launch **EDR4**. In the startup window, press **Connect**.

- In the **Controls** widget:
  a. Open the **Voltage Range** dropdown (▼)
  b. Select:

     i. **700 mV – Ultra Low Noise** for ULN mode, or
     ii. **2000 mV – Low Noise** for LN mode



⚠️ A mismatch between the switch position on the Model Cell and the software setting will produce incorrect measurements.

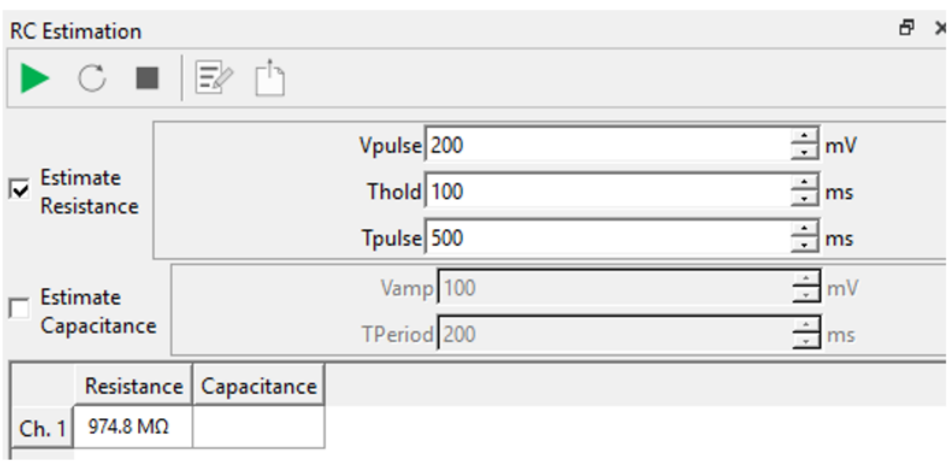
For the 10MHz device, ignore the previous points as no configuration of neither the flow cell nor of the voltage range is needed.

- Open the **RC Estimation** widget. Tick **Estimate Resistance** ☑. Set the stimulus parameters as shown in the reference screenshot.

  Press **Play** (▶) to start the measurement.

  A periodic square-wave stimulus will be applied and the estimated resistance (R) will be reported.

  Given the ±30% tolerance of the Model Cell resistor, the measured value must be within **700 MΩ – 1300 MΩ**

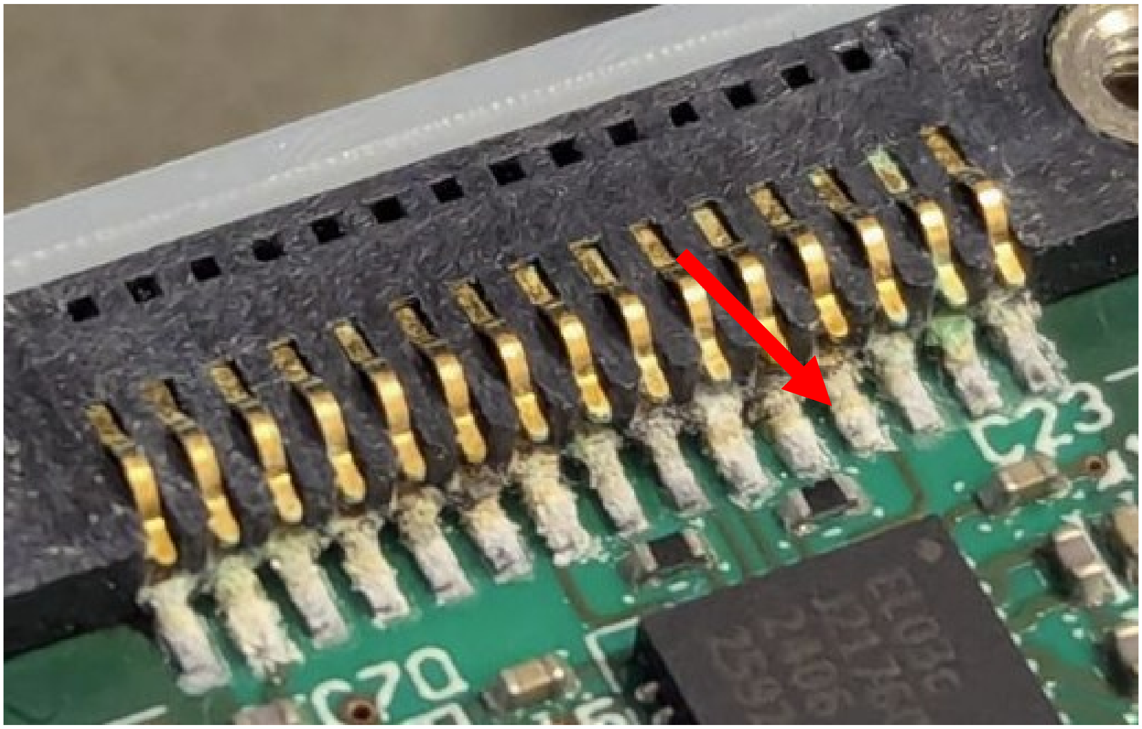


For the 10MHz device, use the IV graph tool, available in EMCR software, to measure the resistance. This can be done, for example, by testing a few voltages (e.g. ±20, ±40, ±60, ±80 and ±100 mV) and fitting the data with a linear equation using the dedicated button. For more details on the IV graph tool please see this guide at page 4.

Visual examples of electrolyte-induced damage to the electronics

When electrolyte reaches the amplifier electronics, it creates unintended conductive paths between adjacent contacts or PCB traces. As the liquid dries, dissolved salts crystallize on the metal surfaces. These residues, along with corrosion products formed by the interaction between the electrolyte and exposed copper layers, increase leakage currents, destabilize the baseline, and raise the noise level.

The images below illustrate typical examples of contamination and corrosion caused by electrolyte intrusion in the eNPR 100 kHz and 10 MHz amplifiers.



These images show severe contamination caused by electrolyte leakage. In addition to crystallized salt deposits, green and blue-green corrosion products are visible around the gold-plated contacts. These residues are typical of copper chloride compounds formed when chloride-containing electrolyte solutions reach the connector area.