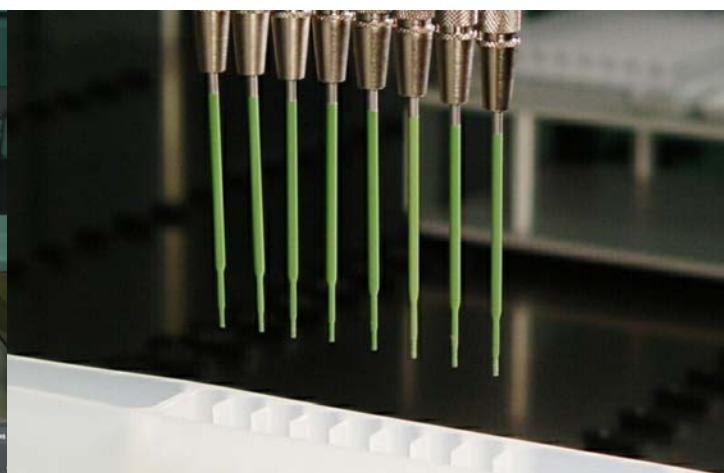
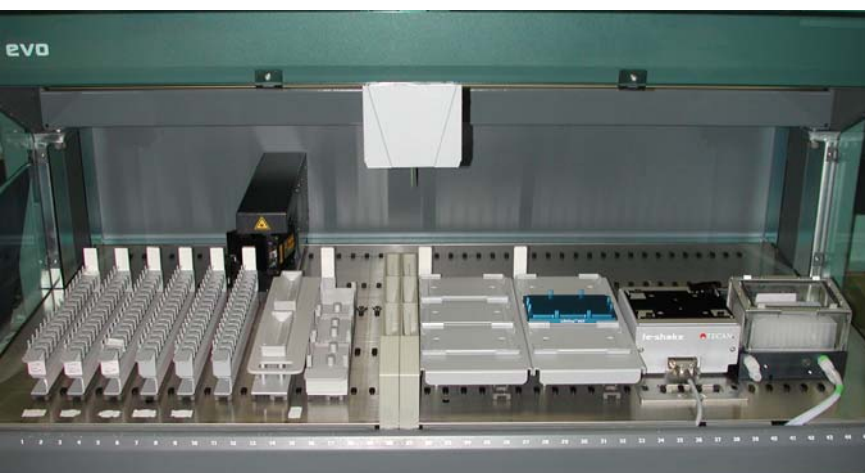


Elimination of amplifiable nucleic-acid carryover from fixed tips on an automated liquid handler in a forensic DNA laboratory

Method validation study



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Introduction

Most fluid-filled automated liquid handlers, or pipetting robots, can be configured with either adapters for disposable tips or fixed, washable tips. For laboratories with moderate to high-throughput processes, fixed tips are often preferable, for two reasons. First, disposable tips initially present on a robotic workstation are consumed and must be re-supplied, either limiting the length of unattended operation between manual replacement of tips, or requiring the dedication of valuable space on the pipetting area of the liquid handler for the tips and logistics devices to supply them. Second, the ongoing purchase of disposable tips results in much higher operating costs than those of the alternative, fixed tips. Disposable tips also present logistical challenges of supply management and

storage, and have a greater environmental impact in the form of waste plastics.

Fixed tips are preferable in many cases; however, the critical requirement for the use of fixed tips is that they may be washed until they are free of any sample materials, in order to prevent cross-contamination of subsequent samples. While some biological assays are relatively insensitive to very small amounts of contamination, nucleic acid amplification techniques such as polymerase chain reaction (PCR) exhibit a response that is not linearly related to the amount of contamination, so that a proportionally small amount of contaminant may dominate the amplified products after PCR. Manual PCR processes traditionally use disposable tips, and, to prevent aerosols within the barrel of the manual pipettor from contaminating subsequent samples, these tips often contain aerosol-resistant filters.

PCR is used in the analysis of human DNA samples toward the generation of genetic profiles from crime scene samples to incriminate or exonerate suspects. For forensic evidence to be useful in the criminal justice system, there must be no question of sample cross-contamination. At first glance, the extremely rigorous requirements for sample integrity would suggest the use of disposable tips. However, DNA identity laboratories more frequently operate at throughputs for which

use of fixed tips is highly preferable for the reasons outlined above. Such laboratories must validate their processes according to standards commonly accepted by the forensic community; and the same high quality standards accepted for laboratories that submit samples to searchable government databases. This application note presents experiments performed by the Research and Development group affiliated with the National DNA Databank of the RCMP^{1,2} to demonstrate that amplifiable material may be eliminated from fixed tips with a protocol of flushing, exposure to bleach solution and washing. The results demonstrate that even after concentration and amplification, blank control samples remain blank and trace DNA samples show expected profiles revealing no carryover of nucleic acid.

Materials and methods

Samples – Swabs with large aliquots of blood (20 µL or 40 µL), buccal swabs and vaginal swabs spiked with 20 µL of semen were purposely used in these studies since they normally yield large amounts of DNA and could challenge the robot tip washing routine. Alternatively, sample batches were created with a variety of biological samples (blood swabs +/- soil [different blood aliquots], bloodstains on black denim, cigarette butts, chewing gums, trace swabs) resembling a true casework sample batch. Blank samples (RCMP Lysis Buffer pH 8.0) were included in all experiments to test the effectiveness of the wash routine in preventing carryover during the automated “direct” or “differential” DNA extraction (used for sexual assault cases) processes and automated DNA quantification process developed at the RCMP.

DNA Quantification – All extracted DNA samples and blank samples were quantified by real-time PCR (Q-PCR) using the AB Quantifiler™ Human DNA Quantitation assay (Applied Biosystems, Foster City, CA) on an ABI Prism® 7000 Sequence Detection System (7000 SDS software v1.0 for real-time data collection and analysis) as outlined in the AB draft protocol. The K562 DNA (Promega Corporation, Madison, MI) was used as the quantification standard in this assay.

Detection of human DNA by Amplification – Human-specific DNA was amplified using the AmpF/STR® Profiler Plus™ PCR Amplification kit (Applied Biosystems, Foster City, CA) with 0.5 ng of target DNA in 15 µL volumes. Amplifications were set up by the robot in 96-well plates and carried out in a DNA Engine™ PTC-200 Peltier thermal cycler (MJ Research Inc., Waltham, MA) using the following cycling program: 95°C, 11 min followed with 28 cycles of denaturation for 60 sec. at 94°C, annealing of primers for 90 sec at 59°C and extension for 90 sec at 72°C. A final extension at 60°C for 45 min followed by an overnight incubation at room temperature was also included. Blank samples (60 µL eluate in low TE pH 9.0) were subjected to filtration through Montage® PCR Filter Units (Millipore, Bedford, MA) according to the manufacturer's protocols. Filtered material was recovered in 20 µL of low TE buffer pH 7.5 and this volume further reduced to 6 µL by vacuum centrifugation before the addition of 9 µL of cocktail mix for short tandem repeat (STR) amplification.

Detection of STR Profiles – Amplified products (1 µL) were robotically mixed with 0.5 µL GeneScan® 500 and 20 µL of HiDi formamide (Applied Biosystems) and analysed by capillary electrophoresis on the ABI Prism 3100 Genetic Analyzer (Applied Biosystems). Samples were electrokinetically injected in 10 sec at 3 kV and electrophoresis was carried out at 15 kV. Alternatively, amplified products (1.5 µL) were mixed with 4 µL denaturing loading buffer (20 mg/mL blue dextran, 7.3 M urea, 2X TBE, 20 mM EDTA) and 0.5 µL GeneScan 500 for analysis on the ABI Prism 377 DNA Sequencer, and a 1.5 µL aliquot was loaded on a 4% (19:1) polyacrylamide gel containing 6M urea prerun at constant voltage (1000 V) for 30 min and equilibrated to 51°C. Electrophoresis was conducted for 2.5 hrs at constant voltage (3000 V) in TBE buffer with the laser power set at 40 mW.

Profile determination was performed using GeneScan Analysis 3.7 and Genotyper® 3.7 programs (Applied Biosystems) for samples run on capillaries and GeneScan Analysis 3.1 and Genotyper 2.5 for samples run on gels. The peak detection threshold used during AmpF/STR Profiler Plus™ profile analysis and interpretation was set at 20 relative fluorescence units (RFUs) for both the ABI Prism 377 DNA Sequencer and ABI Prism 3100 Genetic Analyzer to maximize the detection of peaks in all samples including blanks.

Robotic configuration – Tests were performed on a Tecan Genesis 150 and Tecan Freedom EVO® 150 equipped with eight liquid channels, low volume tubing, 2.5 ml syringes and low-volume tips (P/N 30002384, formerly 71-725 and TER-H564, Low Volume, Adjustable, Short, Teflon Coated). **Wash stations** – Two standard wash stations were used in the sections of this report entitled “Inactivation of residual DNA with bleach solution” and “No carryover detected in concentrated, re-amplified DNA”. Two customized wash stations were used in the section entitled “Improvements to the throughput of the wash procedure” (Tecan U.S. P/N 30011696, smaller well sizes and bottom drains, Teflon).

Bleach – Sodium hypochlorite (LAVO Inc., Montréal, QC, Canada) was used in a final concentration of 2 % (stock from the manufacturer at 10.8 %) to prevent sample cross-contamination. **Disposable tip replacement timing**

calculations – The tip replacement cycle was calculated as the average time from completion of a dispense step to the time at which tips are reloaded and available to begin a subsequent aspiration of a new liquid. Note that a flush of the liquid system to regenerate the liquid column is recommended every six pipetting steps even in the case of disposable tips; this time is included in the average disposable tip replacement cycle time. In addition, periodic replenishment of disposable tips may be done via manual intervention or robotically from shelves or devices such as stackers or carousels; the additional reduction in throughput from these interventions is significant, but varies according to the exact implementation and protocol, and is not included here.

Results

Validation of the washing and bleach-treatment protocol

The liquid handlers currently used by the RCMP, i.e. the Tecan Genesis and Tecan Freedom EVO, have eight liquid channels filled with a system liquid. Movement of this liquid is driven by electronic diluters and syringes, which move the column of system liquid upwards and downwards in tubing connected to the fixed or disposable tip. An air gap is maintained to separate the system liquid from the liquid being pipetted. To aspirate a liquid, the tip is placed into the vessel containing the liquid, then the dilutors move the hydraulic liquid up, also moving the sample to be aspirated into the tip. This process is reversed to dispense the liquid into a destination vessel. To wash the tips, the tips are placed above a waste station, and system liquid is pumped out of the tubing, through the fixed tip via a high-speed diaphragm pump (Figure 1a); the syringes are bypassed during washing. The tips are then moved to a cleaning station with eight individual wells in which the tips are inserted. In the standard wash station, these wells do not have openings at the bottom; the wells are filled by flowing water through the tips using the diaphragm pump and then overflowing into a side well connected to the waste. This allows flow-through cleaning of both the inside and outside of each well, diluting away any sample remaining in or on the pipetting tip.

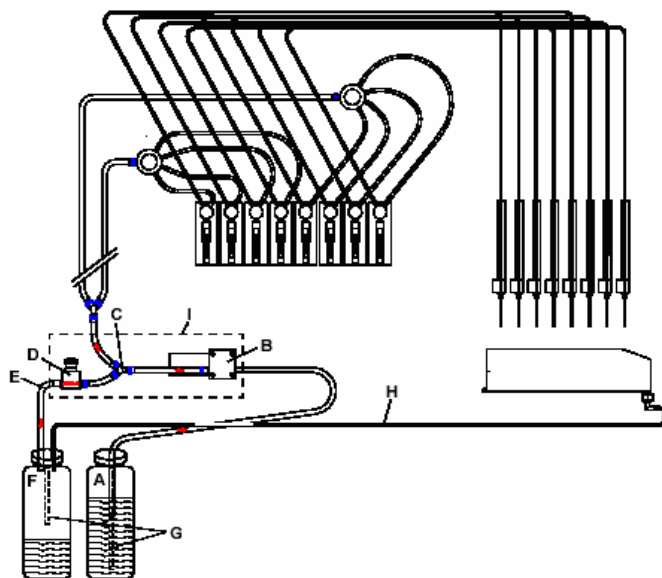


Figure 1a Diagram of the standard wash station
 A. System liquid container. B. Fast wash pump (diaphragm pump, or FAWA). C. 1:2 Distributor. D. Pressure relief valve. E. Bypass tubing (from pressure relief valve). F. Waste container. G. Licos tubes (not installed on instruments in this study). H. Waste tubing from wash station. I. These components comprise the Fast wash option (FWO) or Monitored pump option (MPO). Figure adapted from Freedom EVO Operating Manual, 392886V3.0.



Figure 1b Standard wash stations. The front and rear sections are the deep and shallow wash stations, respectively; the middle section is the waste.

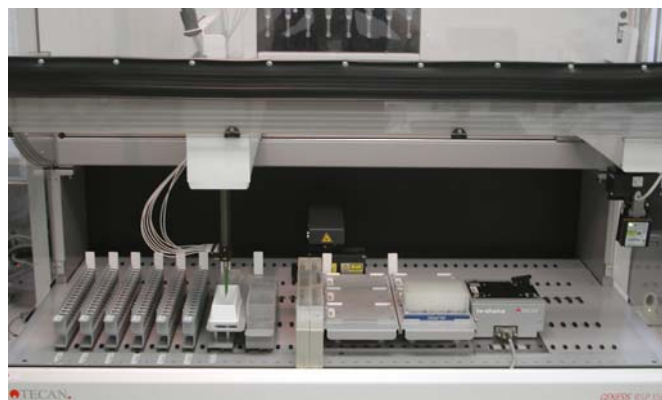


Figure 1c Genesis worktable with two standard wash stations.

Inactivation of residual DNA with bleach solution

Tecan Genesis	Tecan Freedom EVO
Step 1. Waste reservoir; flush: 4 mL; first wash station referred to as the “dirty” wash station	Step 1a. Waste reservoir; flush: 3 mL; first wash station referred to as the “dirty” wash station
	Step 1b. Waste reservoir; flush: 1 mL; second wash station referred to as the “clean” wash station
Step 2. Aspirate 2 % bleach from 200 mL trough: 5X 400 µL or 5X 1000 µL or 5X 250 µL depending on previous volume pipetted in the process	Step 2. Aspirate 2 % bleach from 200 mL trough: 5X 400 µL or 5X 1000 µL or 5X 250 µL depending on previous volume pipetted in the process
Step 3. Shallow reservoir of the “dirty” wash station: 10 mL	Step 3. Shallow reservoir of the “dirty” wash station: 10 mL
Step 4. Shallow reservoir of the “clean” wash station: 10 mL	Step 4. Shallow reservoir of the “clean” wash station: 10 mL

Table 1 Summary of wash conditions for Tecan Genesis and Tecan Freedom EVO

The modified wash procedure used by the RCMP treats the pipetting tips with bleach to inactivate any nucleic acid. After an initial flush in the waste reservoir, a volume of 2 % sodium hypochlorite was aspirated and mixed five times; the volume chosen was equivalent to the previously pipetted volume to ensure all the tip and tubing surfaces exposed to the sample were bleach-treated. Residual bleach solution was then removed by a wash procedure, using two wash stations, rather than one (Figures 1b, 1c). This wash was initiated in the shallow reservoir of the first, or “dirty”, wash station and ended in the shallow reservoir of the second, or “clean”, wash station for optimal cleanup and to obviate the possibility of re-introduction onto the tips of any trace nucleic acid that had been washed into the initial “dirty” wash station. Volumes of wash solutions are summarized in Table 1 for both the Tecan Genesis and Freedom EVO robotic workstations. These were empirically determined such that the residual bleach was diluted well beyond the threshold at which it began to inhibit subsequent STR amplification reactions.

To demonstrate that the above wash/nucleic acid inactivation protocol was effective, human biological samples yielding high quantities of DNA (average of 500-1000 ng total DNA based on Q-PCR quantification) were positioned into alternate wells with blanks in a checkerboard pattern across a 96 deep-well plate or in alternate columns with blanks in a zebra-stripe format (Figure 2a) and were extracted and quantified using the automated protocols optimized at the RCMP (DNA extraction based on the Promega DNA IQ™ magnetic bead system [Promega Corporation, Madison, WI] and Q-PCR). All blank samples (60 µL eluate in low TE pH 9.0) were concentrated using Montage PCR Filter Units and the presence of nucleic acid carryover acid evaluated by STR amplification. If the wash protocol was effective, wells corresponding to blank samples should not contain amplifiable DNA, whereas wells that contain DNA should result in strong signals, indicating that the wash/bleach protocol has not inhibited the PCR reaction.

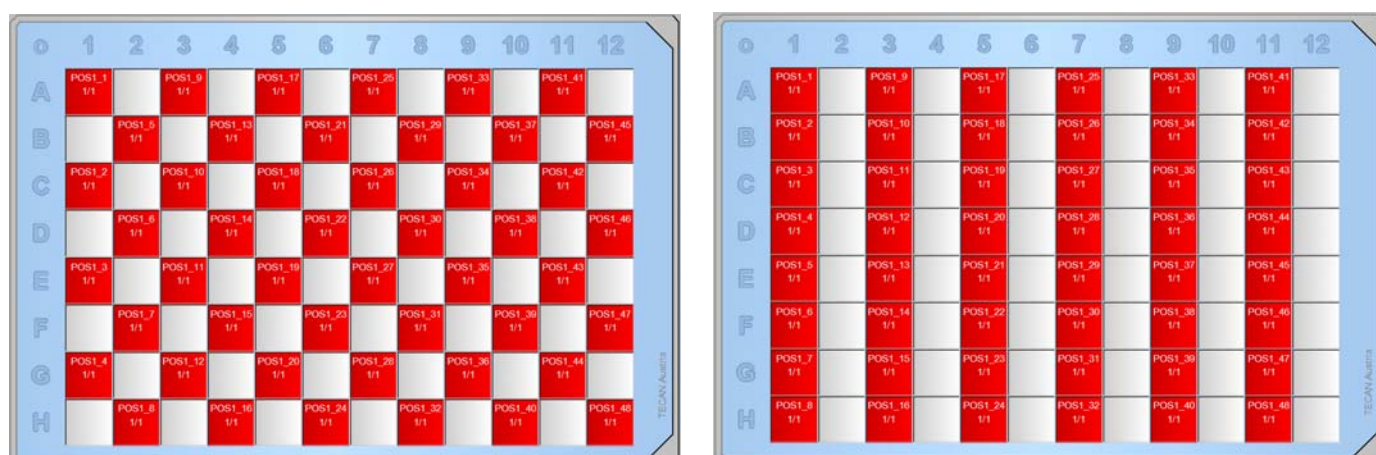


Figure 2a Plate layouts for cross-contamination experiments. Red squares represent biological samples (positive controls). White squares represent blank controls. Left panel: “Checkerboard pattern”. Right panel: “Zebra-stripe pattern”.

When these checkerboard- and zebra stripe-format experiments were performed, of 33 plates containing 993 blank wells, no carryover DNA was detected by Q-PCR. During the validation of the wash/bleach protocol, an additional 341 similar blank controls were analyzed and found to have no detectable nucleic acid using these criteria, for a total of 1334 blank controls with no carryover.

To further validate the wash/bleach routine, a subset of 403 of the blank controls was further subjected to STR profile analysis (Table 2, left column). No STR profile was derived from the blank samples using a 1X or 10X boosted aliquot³ (i.e. using 40 % of the amplified extracts [6 µL of a 15 µL PCR reaction containing the entire blank eluate, filtered and concentrated] vacuum-centrifuged and reconstituted in 4 µL of gel loading buffer from which a 1.5 µL aliquot was loaded) on the ABI Prism 377 DNA Sequencer and a peak detection threshold of 20 RFUs.

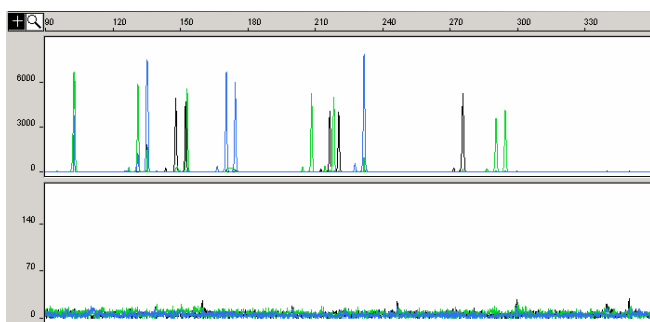


Figure 2b Representative electropherogram from a biological sample (top panel) and the blank control pipetted with the same fixed tip immediately afterward during the extraction process (bottom panel). The washing procedure included the bleach step. The numerical scale on the left of each tracing is relative fluorescent units (RFUs) during STR detection.

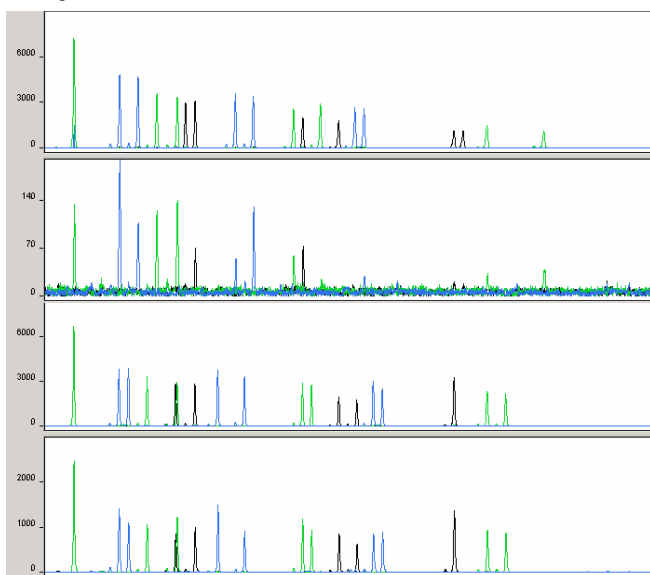


Figure 2c Two sets of representative electropherograms from experiments in which the bleach step was omitted from the wash procedure. Each set consists of a biological sample (top panels) and the blank control pipetted with the same fixed tip immediately afterward during the extraction process (bottom panels). The numerical scale on the left of each tracing is relative fluorescent units (RFUs) during STR detection.

Similarly, no profile was observed from the blank samples run on the ABI Prism 3100 Genetic Analyzer. The 1941 AmpF/STR Profiler Plus™ profiles generated from the biological samples extracted alongside the blanks were consistent with expected results. An example of the resulting data is shown in Figure 2b. In control experiments, it was demonstrated that cross-contamination could routinely be detected in the blanks if the bleach step was eliminated but the flush and wash steps in the shallow reservoirs retained (Table 2, right column). The inclusion of bleach is thus critical for prevention of carryover of amplifiable material. Two example profiles are shown in Figure 2c.

The wash/bleach routine was determined to be effective in preventing cross-contamination from samples yielding greater than 1000 ng DNA such as on vaginal swabs spiked with semen and buccal swabs. In addition, the bleach routine was shown to have no adverse effect on the recovery of trace amounts of DNA. In some instances, as little as 80-100 pg DNA was recovered from such samples and produced either full or partial STR profiles (see next section).

	With wash/bleach procedure ^a	With wash/no bleach procedure ^b
Biological samples subjected to STR amplification	1941	38
Biological samples for which the expected STR profile was derived	1941	38
Blank samples subjected to STR amplification	403	31
Blank samples for which an STR profile was derived	0 ^c	31 ^d

Table 2 Effectiveness of the bleach step in preventing contamination.

^a Includes a flush step (4 mL) in the waste followed with 5 mixes in the bleach trough followed with a wash step (10 mL) in the shallow reservoir of the “dirty” wash station and a wash step (10 mL) in the shallow reservoir of the “clean” wash station.

^b Includes a flush step (4 mL) in the waste followed with a wash step (10 mL) in the shallow reservoir of the “dirty” wash station and a wash step (10 mL) in the shallow reservoir of the “clean” wash station.

^c No alleles detected using a threshold of detection of 20 RFU.

^d Blank samples exhibited sporadic alleles or full profiles matching samples previously pipetted by the robot.

No carryover detected in concentrated, amplified DNA

Control samples for criminal or standard databases are taken under supervision with a specific sample collection kit to optimize yield and quality of DNA in order to generate a genetic profile. Samples obtained from crime scenes or crime victims, generally termed casework samples, may be in trace amounts and yield minimal amounts of DNA. For these types of samples, the automated protocols developed by the RCMP include a concentration step using Te-Vacs filtration units followed with amplification of the concentrated material in order to possibly recover a profile. During validation of the wash/bleach routine, approximately 3 % of samples displayed low DNA concentrations (between 0.004 ng/ μ L and 0.008 ng/ μ L) but total target amounts of 0.2 ng to 0.5 ng DNA that required concentration prior to STR analysis. All of these were successfully amplified to give profiles. No extraneous or exogenous peaks were detected in the 74 generated profiles. The wash protocol therefore was capable of eliminating carryover to permit sample concentration when necessary and allow generation of full or partial profiles from trace samples.

Improvements to the throughput of the wash procedure

The wash protocol shown to be successful involves four steps: 1) a flush (4 mL) in the waste of the first wash station, 2) aspiration and dispense of bleach solution (5 mixes), 3) a wash (10 mL) in the shallow reservoir of the “dirty” wash station, and 4) a wash (10 mL) in the shallow reservoir of the “clean” wash station. This procedure was shown to be effective above; however, the washing protocol takes approximately 1.8-2.1 minutes per cycle (i.e. flush, bleach, wash twice) depending on the volume of bleach aspirated. This compares to a tip replacement cycle averaging 16 seconds (0.27 min) for disposable tips (not including procedures for replenishing consumed tips). For the automated DNA extraction protocol used at the RCMP, washing constituted approximately 64 minutes of the 2 hours and 50 minutes required to process 88 samples (this time includes sample tracking and human intervention steps during extraction and final elution steps not performed on the robot deck; these steps together take 30 min), or 38 % of the total processing time. Modifications were therefore made to the initial wash protocol toward the goal of reducing overall washing time and thereby increasing process throughput.

Three modifications were taken to reduce the wash times while retaining their effectiveness. First, the wash times are lengthy because the flow rate of the diaphragm pump must be reduced to values ranging from 15 % to 35 % of the maximum setting when using 1 mm inner diameter (ID) tubing (“low volume” tubing; standard tubing is 1.5 mm ID) to avoid excessive pressure during washing. However, it was empirically determined that the diaphragm pump flow rate could be increased to 55 % without resulting in excess pressure; the flow rate of the pump was set at 50 %. At this setting, the flow rate through the tip is approximately 0.46 mL/sec.

Second, active wash stations were employed. The manufacturer offers a low volume active wash station with reservoirs that are much shorter and have much smaller diameter wells (well capacity of 200 μ L instead of 400 μ L) (Figure 3a). The wells therefore fill up faster, and the flow is more turbulent. In addition, the wells of the active low volume wash station are connected to a fluid channel via small holes through the bottom. When the diaphragm pump is used with a low diameter tubing system, approximately 60 % of the system liquid flows not through the wash station, but out a pressure relief valve designed to prevent tubing ruptures. In the low volume wash station, this overflow is directed into the channel connected to the cleaner wells, allowing them to fill more quickly, providing more effective washing to the upper portions of the outside of the pipetting tip (Figure 3b).

Because there are two wash stations used in the wash protocol, the effluent from the overflow valve was split and directed to both wash stations using a simple Y-connector; thus the wash station not in use also receives additional flow-through washing during a wash, further reducing the possibility that contaminants can remain from the previous wash step. One-way valves (“check valves”) were employed to prevent backward draining of the liquid remaining in the wash station into the system liquid reservoir. The addition of the active low volume wash stations increased the volume of wash liquid that the tips encounter during a given time.

The third improvement was to optimize wash volumes for specific steps of the protocol. The wash procedure initially developed was designed to prevent carryover in the worst-case scenario, specifically the transfer of ~1 mL volume of lysate solutions on instruments performing DNA extractions. This wash procedure was used for all pipetting steps involving samples, even if the volume pipetted was considerably smaller. The volumes in a given wash were optimized by adjusting the wash volume to meet a minimum “interior tip rinse factor” of 8, and a “tip exterior rinse volume” of 4 mL, based on the original wash parameters. In addition, the wash step commands were adjusted so that 60 % of the cleaning volume was directed to the “dirty” reservoir (first wash station), to reduce exposure of the “clean station” to potential contaminants. It was also determined empirically that the number of mixes in the bleach solution could be reduced from five to three. Finally, further studies on the washing parameters for the worst-case lysate step were carried out; the implementation of changes suggested by these studies enabled some reduction in the large volumes used for this step. The improved washing parameters are summarized in Table 3.

With these changes, the wash cycle (flush, bleach, wash twice) was decreased from the original 1.8-2.1 minutes to 43-60 seconds reducing the overall duration of the washing steps for DNA extraction from 64.5 min to 17.5 min, a time savings of 73 %. With the improved wash protocol, the overall processing time for the automated extraction of DNA from 88 samples was reduced from 2 hours and 50 minutes to 2 hours (includes sample tracking and human intervention steps during extraction and final elution steps not performed on the robot deck; these steps together take 30 min).

The validation experiments to show that no nucleic acid was carried over were repeated using the improved wash/bleach routine. In total, nine 96-well plates containing buccal swabs or vaginal swabs with semen (see Materials and Methods for details) were processed along with 288 blank samples. No STR profile was developed from any of the blanks tested indicating that the new modifications did not impact on the ability to achieve a “no-contamination” status.

Tecan Genesis	Tecan Freedom EVO
Step 1. Waste reservoir; flush: 4 mL; first wash station referred to as the “dirty” wash station	Step 1a. Waste reservoir; flush: 3 mL; first wash station referred to as the “dirty” wash station
	Step 1b. Waste reservoir; flush: 1 mL; second wash station referred to as the “clean” wash station
Step 2. Aspirate 2 % bleach from 200 mL trough: 3X 400 µL or 3X 1000 µL or 3X 250 µL depending on previous volume pipetted in the process	Step 2. Aspirate 2 % bleach from 200 mL trough: 3X 400 µL or 3X 1000 µL or 3X 250 µL depending on previous volume pipetted in the process
Step 3. Shallow reservoir of the “dirty” wash station: 3 mL (6 mL for lysate column aspiration step ^a)	Step 3. Shallow reservoir of the “dirty” wash station: 3 mL (6 mL for lysate column aspiration step ^a)
Step 4. Shallow reservoir of the “clean” wash station: 2 mL (4 mL for lysate column aspiration step ^a)	Step 4. Shallow reservoir of the “clean” wash station: 2 mL (4 mL for lysate column aspiration step ^a)

Table 3 Summary of improved wash conditions using low volume wash stations for Tecan Genesis and Tecan Freedom EVO

^a “lysate column aspiration step” refers to the removal of the 1 mL lysate column after capture of the DNA on the DNA IQ™ magnetic beads.

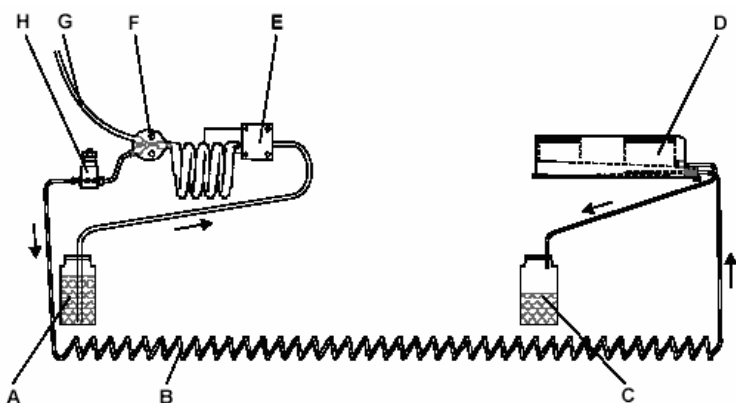


Figure 3a Diagram of the low volume wash station. A. System liquid container. B. Fill tubing (from pressure relief valve). C. Waste container. D. Low volume wash station. E. Fast wash pump. F. 1:2 Distributor. G. Tubing to dilutors. H. Pressure relief valve. Figure adapted from Freedom EVO Operating Manual, 392886V3.0.



Figure 3b Revised setup with low volume wash stations.

Conclusions

The studies conducted by the RCMP National Services and Research and National DNA Data Bank demonstrate that amplifiable material may be effectively removed from fixed, washable tips on an automated liquid handler using a simple 2 % bleach solution. Further improvements to the washing setup and procedure result in washing times that are comparable to disposable tips. The RCMP has employed these systems to process over 3,299 samples from break-and-enter cases and over 11,156 violent crime casework samples over the last three years. Casework samples are by nature irreplaceable and of unknown concentration and state of biological degradation when they arrive for analysis. For samples immobilized on solid supports, a less extensive wash procedure than that described above may prove effective. For instance, the approximately 120,000 convicted offender samples submitted to date to the National DNA Data Bank of Canada on Whatman FTA[®] Sample Collection Cards (Fitzco Inc., Spring Park, MN) have been processed using a simpler wash procedure using only one standard wash station¹. No bleach is required for FTA[®] punched disks and a wash cycle comprised of a flush (2 mL) step in the waste reservoir followed with a wash step (2 mL) in the shallow reservoir with the diaphragm pump set at 15 % is sufficient to prevent cross-contamination (over 5700 blank samples analyzed).

The use of fixed tips and a wash/bleach procedure have several advantages over the use of disposable tips. The wash stations occupy less space on the worktable of the liquid handler than even the minimum number of disposable tip carriers, and the overall throughput is similar to that when using disposable tips. The initial investment in wash stations required for the bleach wash protocols described above is minimal and comparable to or less than that for carriers for disposable tips. The operating costs consist only of the supply of water and bleach solution, compared to outlays of hundreds, thousands, or in the case of very high-throughput laboratories, tens of thousands of dollars worth of disposable tips per month.

These studies indicate that even laboratories working with nucleic acid amplification with rigorous requirements for maintaining sample integrity, quality and a high expectation of success can benefit from the advantages of lower operating costs, reduced plastic consumption and supply management associated with automated liquid handlers configured with fixed, washable tips.

This paper is intended for forensic and research use only, and is not intended for application to diagnostic procedures, human clinical trials, or blood and/or plasma donation screening. The permission to reproduce RCMP results in this publication does not imply that use of the techniques herein is limited to Tecan instruments, nor does it constitute commercial endorsement of Tecan instruments by the RCMP.

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