

Electronic Supplementary Information

An automated sequential flow platform for the separation of amine/alkene mixtures

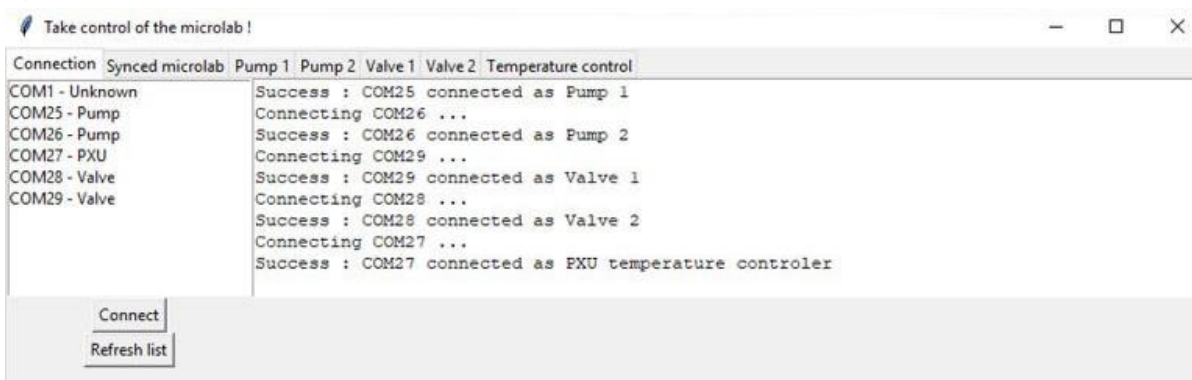
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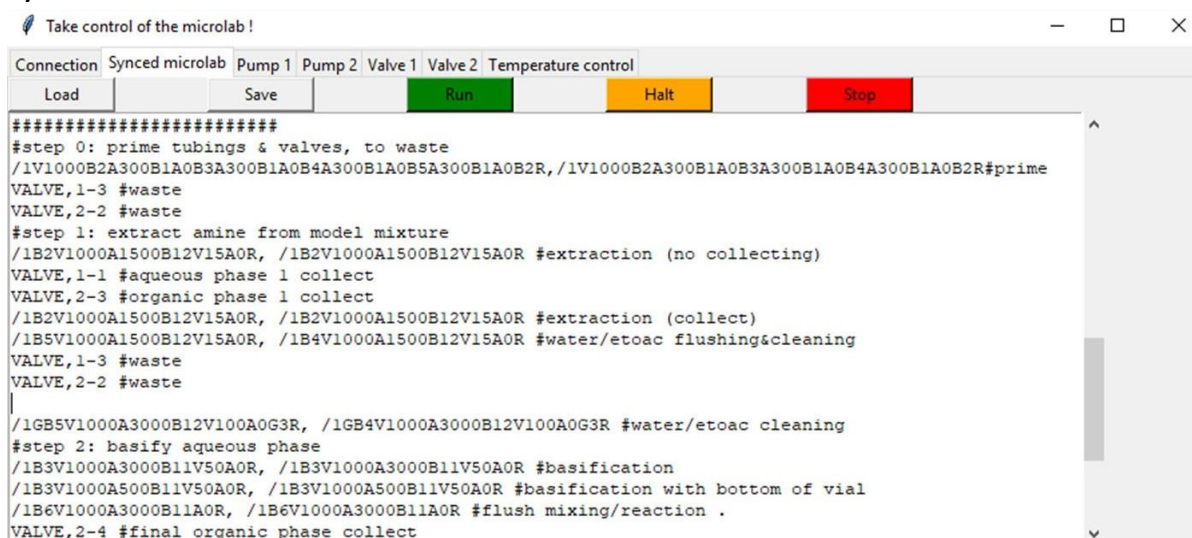
^b Integrated Drug Discovery, Sanofi R&D.

^c Integrated Drug Discovery, Syngene

a)



b)



c)

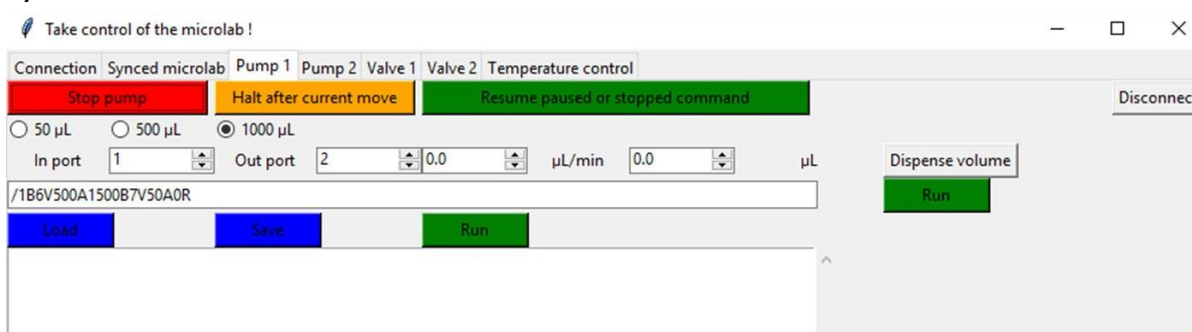


Figure S1 : Snapshots of the GUI, showing the tabs for a) connec,on, b) synchronized control and c) pump control. The connec,on tab displays a list of COM ports to connect (left) and a log file (right). The synchronised tab essentially displays a text entry to upload and run automated processes. The pump control displays dispense commands and text entries to run command lines using the code language specific to the pumps.

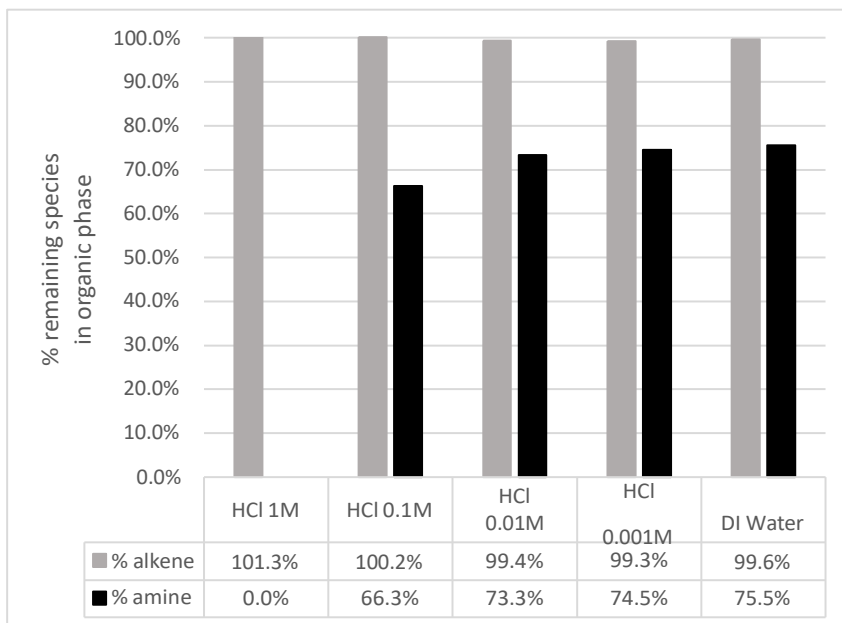


Figure S2 : Remaining cyclohexene and cyclohexylamine in the organic phase after treating the model mixture with aqueous solutions at different HCl concentrations, by batch.

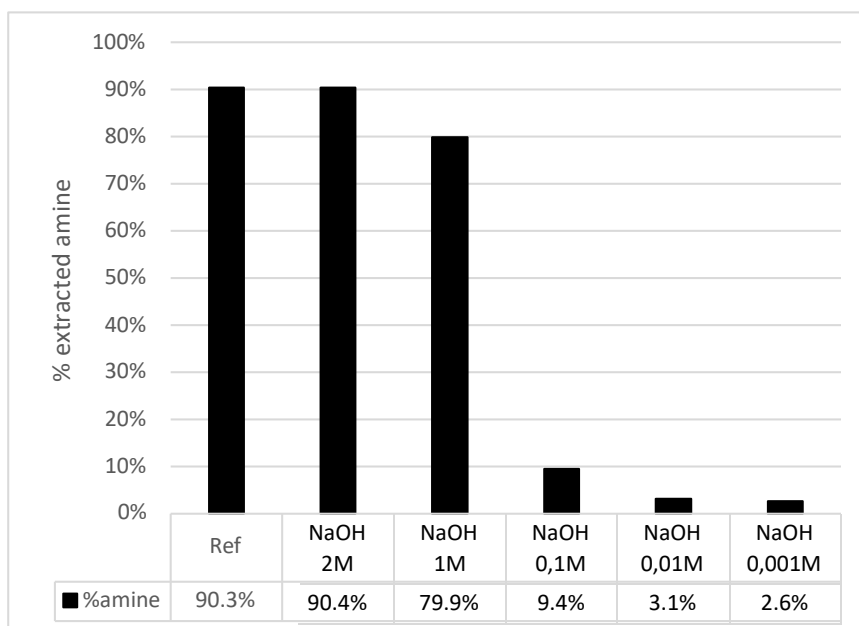


Figure S3 : Extraction efficiency of cyclohexylamine from a mixture mimicking a perfect first step (1 M cyclohexylamine in 1 M HCl), treated with aqueous solutions at different NaOH concentrations followed by addition of EtOAc, by batch.

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#pump 1 :
#b1=waste
#b2=model mixture (1mL)
#b3=aqueous phase 1 (HCl+amine, 1mL)
#b4=aqueous phase 2 (HCl+amine+NaOH, 2mL)
#b5=water
#b6=air
#b11=react;on tubing 500µL
#b12=extract;on tubing 250µL+separator
#pump 2:
#b1=waste
#b2=HCl 1M (1mL)
#b3=NaOH 2M (1mL)
#b4=EtOAc (5mL)
#b5=air
#b11=react;on tubing 500µl
#b12=extract;on tubing 250µl+separator
#valve 1 (aqueous outlet of separator):
#b1= aqueous phase 1 (HCl+amine, idem pump 1 b3)
#b3=waste
#valve 2 (organic outlet of separator):
#b3=waste
#b4=organic phase 1 (collect for study)
#b5=organic phase 2 (collect for study)
#b6=organic phase 3 (final collect)

#step 0: prime tubings & valves, to waste
/1V1000B2A300B1A0B3A300B1A0B4A300B1A0B5A300B1A0B2R,/1V1000B2A300B1A0B3A300B1A0B4A300B1A0B2R#prime
VALVE,1-3 #waste
VALVE,2-2 #waste

#step 1: extract amine from model mixture
/1B2V1000A1500B12V15A0R,/1B2V1000A1500B12V15A0R #extract;on (no collec;ng)
VALVE,1-1 #aqueous phase 1 collect
VALVE,2-4 #organic phase 1 collect
/1B2V1000A1500B12V15A0R,/1B2V1000A1500B12V15A0R #extract;on (collect)
/1B5V1000A1500B12V15A0R,/1B4V1000A1500B12V15A0R #water/etoac flushing&cleaning
VALVE,1-2 #waste
VALVE,2-3 #waste

/1GB5V1000A3000B12V100A0G3R,/1GB4V1000A3000B12V100A0G3R #water/etoac washing

#step 2: basify aqueous phase
/1B3V1000A3000B11V50A0R,/1B3V1000A3000B11V50A0R #basifica;on
/1B3V1000A500B11V50A0R,/1B3V1000A500B11V50A0R #basifica;on with bofom of vial
/1B6V1000A3000B11A0R,/1B5V1000A3000B11A0R #flush mixing/react;on .
VALVE,2-6 #final organic phase collect

#step 3: extract amine to organic phase
/1GB4V1000A3000B12V50A0G2R,/1GB4V1000A3000B12V50A0G2R #extract;on
/1GB4V1000A1000B12V50A0G2R,/1GB4V1000A1000B12V50A0G2R #extract;on with bofom of vial

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Figure S4 : .txt file of commands sent via the microlab soGware to the set-up. The symbol "#" precedes comments. Lines starting with "/" are interpreted by the pumps, with command syntax as provided by the supplier. Lines starting with "VALVE" are interpreted by the valves with custom syntax.