

need to change or adjust component hardware. One embodiment of multiple separation systems interfaced to a single ES source is diagrammed in FIG. 8. A first gradient liquid chromatography system 184 comprises LC gradient pump 185, injector valve 186, manual or auto injector 187, liquid chromatography column 188, switching valve 191, and connecting line 180 to ES probe assembly 172. Similarly, a second gradient LC system 194 comprises LC gradient pump 195, injector valve 196, manual or auto injector 197, liquid chromatography column 198, switching valve 199, and connecting line 179 to ES probe assembly 170. Sheath liquid flow can be delivered through transfer line 192 to ES probe assembly 172 and through connecting line 201 to ES probe assembly 170. Nebulizing gas is delivered through lines 193 and 181 to ES probe assemblies 172 and 170 respectively. In the configuration shown, the following sequence could be used to double the sample throughput with LC-MS analysis using one Electrospray mass spectrometer detector.

[0063] Assume that during each LC-MS run, calibration solution is sprayed continuously from ES probe tip 174 while MS data is being acquired. The LC-MS analytical sequence begins with valve 191 switched so that solution delivered from LC gradient pump 185 is directed to flow through line 189 with no sample solution flow directed to ES probe inlet line 180. With valve 191 switched to this position, column 188 can be flushed or reconditioned after an LC gradient run without introducing contamination into ES source 160. The pneumatic nebulization gas flow to ES probe tip 175 may or may not be turned on depending on how the gas flows in mixing region 182 are initially balanced. Valve 199 is switched so that solution delivered from LC gradient pump 195 flows into transfer line 179 to ES probe assembly 170 exiting at ES probe tip 173. LC column 198 has been reconditioned or flushed and the solution composition being delivered from LC pump 195 is the solution required for initiation of an LC gradient run. Sample is injected from manual or autoinjector 197 into valve 196 and an LC separation is initiated when injector valve 196 is switched from load to run placing the injected sample on line with column 198. Nebulization gas and, if required, liquid layered flow is delivered to ES probe tip 173 in addition to the sample solution. As the LC gradient separation through column 198 proceeds, components eluting from column 198, travel through valve 199 and line 179 where they are Electrosprayed from tip 173. A portion of the ions produced the sample solution during the Electrospray ionization process are subsequently mass analyzed. During and prior to the completion of the analytical gradient LC run which is occurring in LC column 198, column 188 is being flushed, reconditioned, or re-equilibrated and the solution gradient reset for another LC gradient separation. When the LC gradient run through column 198 is complete, valve 199 is switched so that the eluate from LC column 198 flows through line 202 and not through line 179. Alternatively, an additional solvent flow can be supplied through line 200 into line 179 through valve 199 in this switch position to flush line 179 prior to the start of the LC gradient run through ES probe assembly 172. When valve 199 is switched to divert the flow through column 198 to line 202, valve 191 is switched to connect the flow exiting column 188 to line 180 and ES probe assembly 172. If the pneumatic nebulization gas flow to ES probe 172 was turned off while the gradient LC run through column 198 was occurring, it is turned back

on at this point. Nebulization gas supplied through line 181 to ES probe assembly 170 may remain on or be turned off depending on how the spray gas balance in region 182 has been optimized. A sample is injected into injector valve 186 with manual or auto injector 187 and an LC gradient separation begins with LC system 184 when valve 186 is switched from inject to run. Sample bearing solution eluting from column 188 is delivered to ES probe tip 175 through line 180 and is Electrosprayed into ES chamber 161. A portion of the sample ions resulting from the Electrospray process are drawn into vacuum through orifice 164 where they are mass analyzed. When the gradient LC run through LC column 188 is complete, valve 191 is once again switched so that solution flow from LC column 188 is directed to flow through line 189 and the cycle described above begins again. Solution flow can be delivered through line 190 to ES probe assembly 172 to flush line 180 prior to initiating the next gradient run through LC column 198.

[0064] The analytical sequence example described above includes switching between two LC separation systems using one ES-MS detector to increase sample throughput. While one LC column is being flushed after an LC run, an analytical separation is being conducted using a second LC separation system. Sample solution from LC system 194 is delivered to ES source 160 through ES probe assembly 170 and sample solution from LC separation system 184 is delivered to ES source 160 through ES probe assembly 172. A calibration solution can be delivered to ES source 160 through ES probe assembly 171 simultaneously with the Electrospraying of either LC separation solutions to create an ion mixture. A mass spectrum acquired from the resulting ion mixture contains an internal standard peaks which can be used for mass calibration and/or quantitative analysis calculations.

[0065] Several variations to the multiple ES probe embodiment diagrammed in FIG. 8 can be configured. One variation would be to eliminate switching valves 191 and 199 and send the solution flow from columns 188 and 198 directly into ES probe assemblies 170 and 172. This would reduce dead volume and even allow the incorporation of fused silica packed columns as the first layer sample delivery tube configured in ES probe assemblies 170 and 172 exiting at ES tips 173 and 175 respectively. During the column flushing period prior to an LC analytical run, say for ES probe assembly 170, the position of ES probe tip 173 can be moved so that any spray from tip 173, from flow through column 198, would be directed away from mixing region 182 when ES probes 171 and 172 are spraying. Probe tip 173 would then be moved back into position when the analytical separation through column 198 was reinitiated. ES probe tip 175 would then be moved to a position during flushing of LC column 188 such that any spray from tip 175 would not be directed into mixing region 182. In this second position, any spray from tip 175 during flushing through column 188 would not contribute chemical noise to acquired mass spectra during the LC-MS analysis of samples flowing through LC column 198. The positions of ES probe assemblies 170 and 172 can be changed with automated adjustment means during programmed multiple LC column analysis sequences.

[0066] An alternative and simpler method to recondition or flush LC columns between LC runs through an ES probe assembly without the need to move the ES probe position,