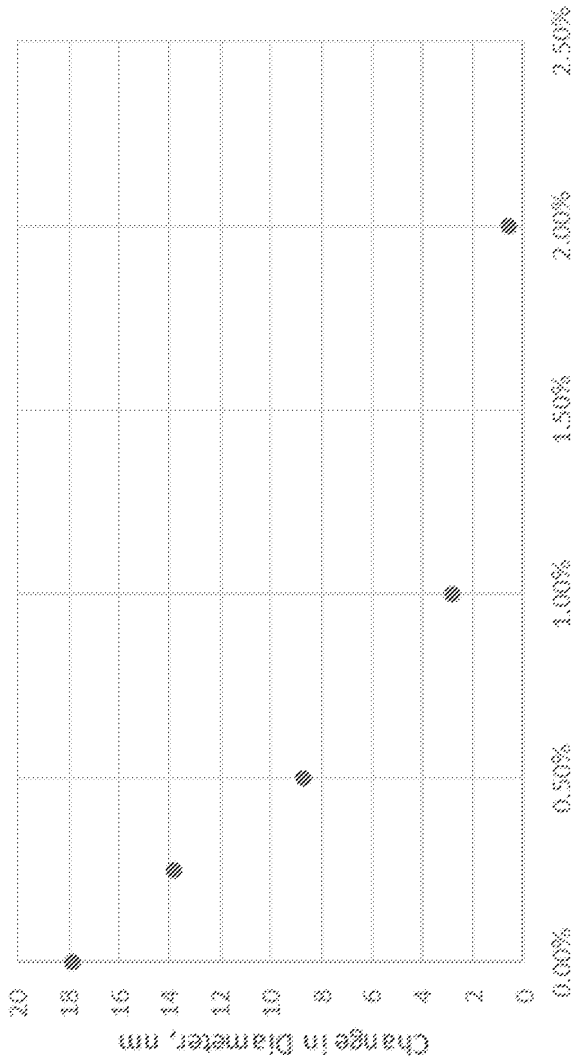

Change in diameter, nm
20
18
16
14
12
10
8
6
4
2
0
0.00%
0.50%
1.00%
1.50%
2.00%
2.50%
mol% PEG

Fig. 1

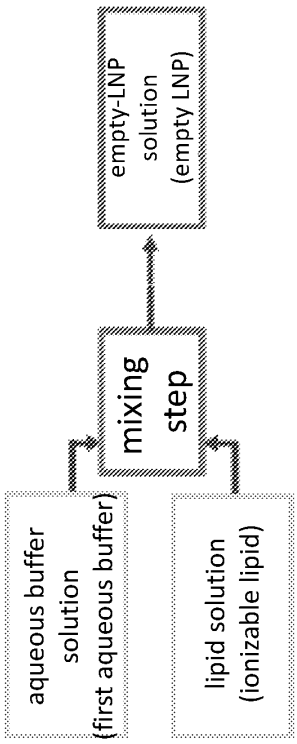

empty-LNP solution (empty LNP)
mixing step
aqueous buffer solution (first aqueous buffer)
lipid solution (ionizable lipid)

Fig. 2

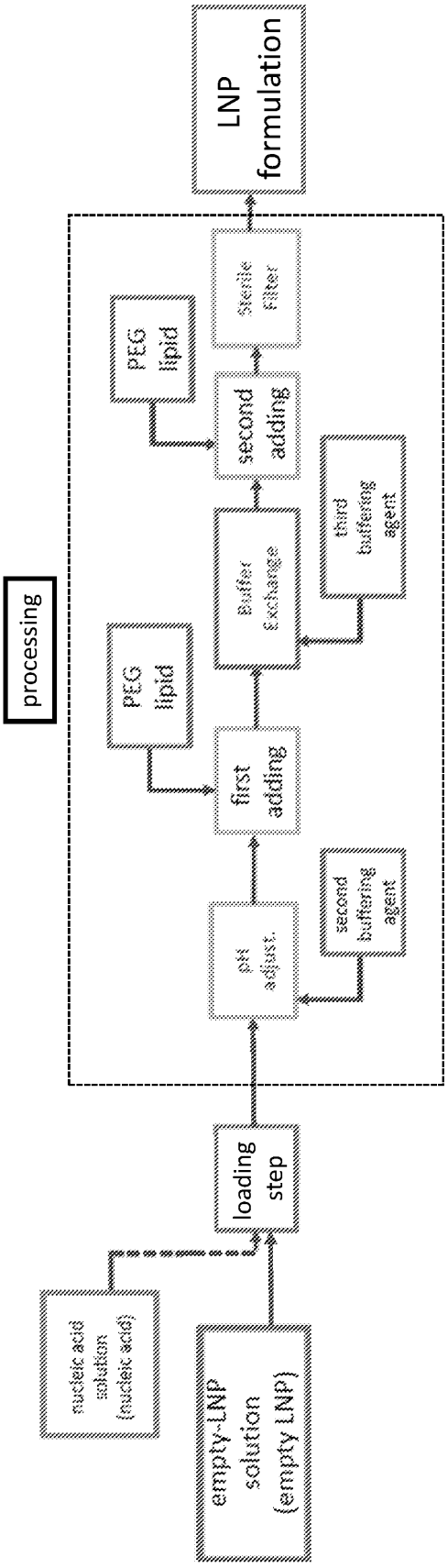

empty-LNP solution (empty LNP)
nucleic acid solution (nucleic acid)
loading step
processing
pH adjust.
second buffering agent
first adding
PEG lipid
Buffer Exchange
third buffering agent
second adding
PEG lipid
Sterile Filter
LNP formulation

Fig. 3

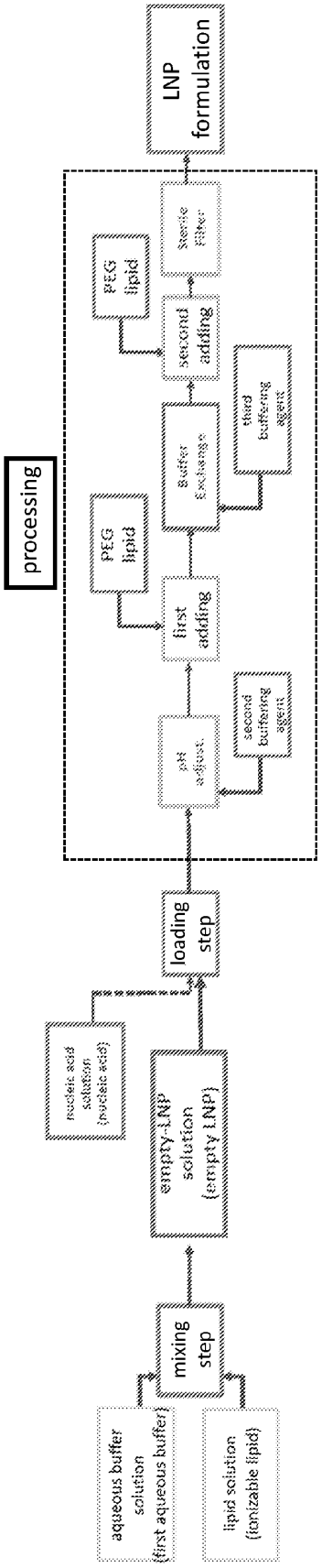

aqueous buffer solution (first aqueous buffer)
lipid solution (ionizable lipid)
mixing step
empty-LNP solution (empty LNP)
nucleic acid solution (nucleic acid)
loading step
processing
pH adjust
second buffering agent
first adding
PEG lipid
Buffer Exchange
third buffering agent
second adding
PEG lipid
Sterile Filter
LNP formulation

Fig. 4

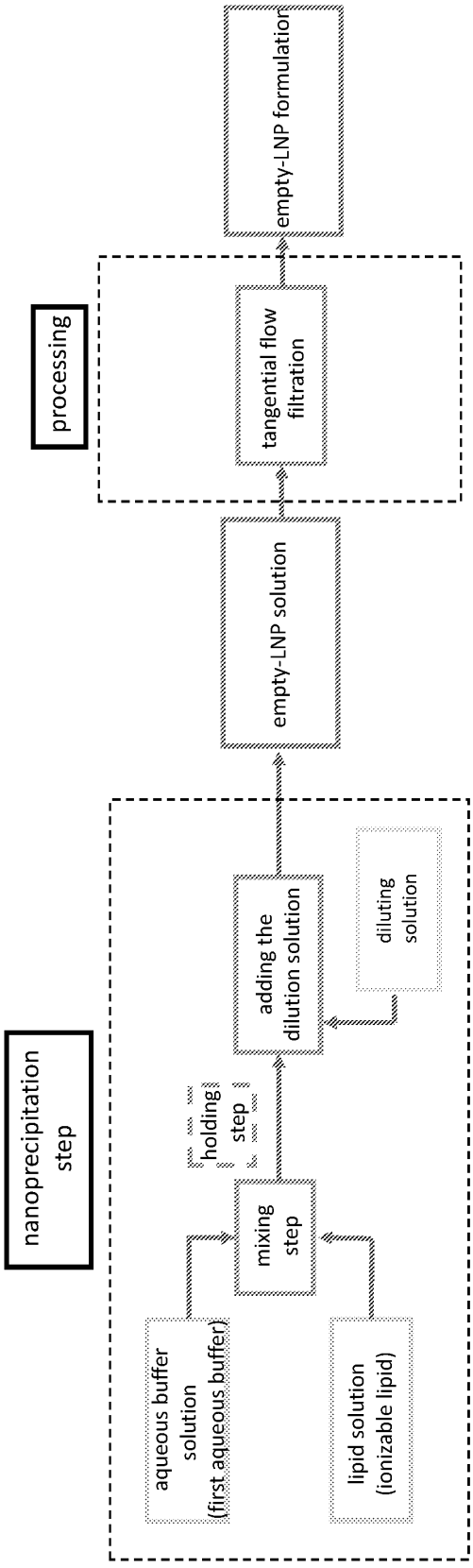

nanoprecipitation step
aqueous buffer solution (first aqueous buffer)
lipid solution (ionizable lipid)
mixing step
holding step
adding the dilution solution
diluting solution
empty-LNP solution
processing
tangential flow filtration
empty-LNP formulation

Fig. 5

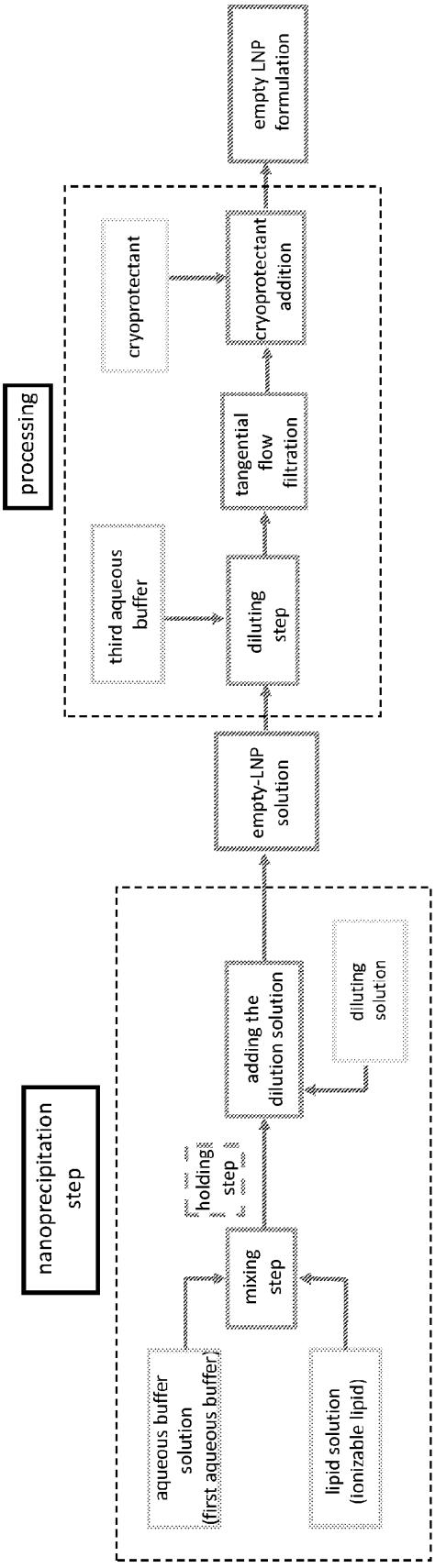

nanoprecipitation step
aqueous buffer solution (first aqueous buffer)
lipid solution (ionizable lipid)
mixing step
holding step
adding the dilution solution
diluting solution
empty-LNP solution
processing
third aqueous buffer
diluting step
tangential flow filtration
cryoprotectant
cryoprotectant addition
empty LNP formulation

Fig. 6

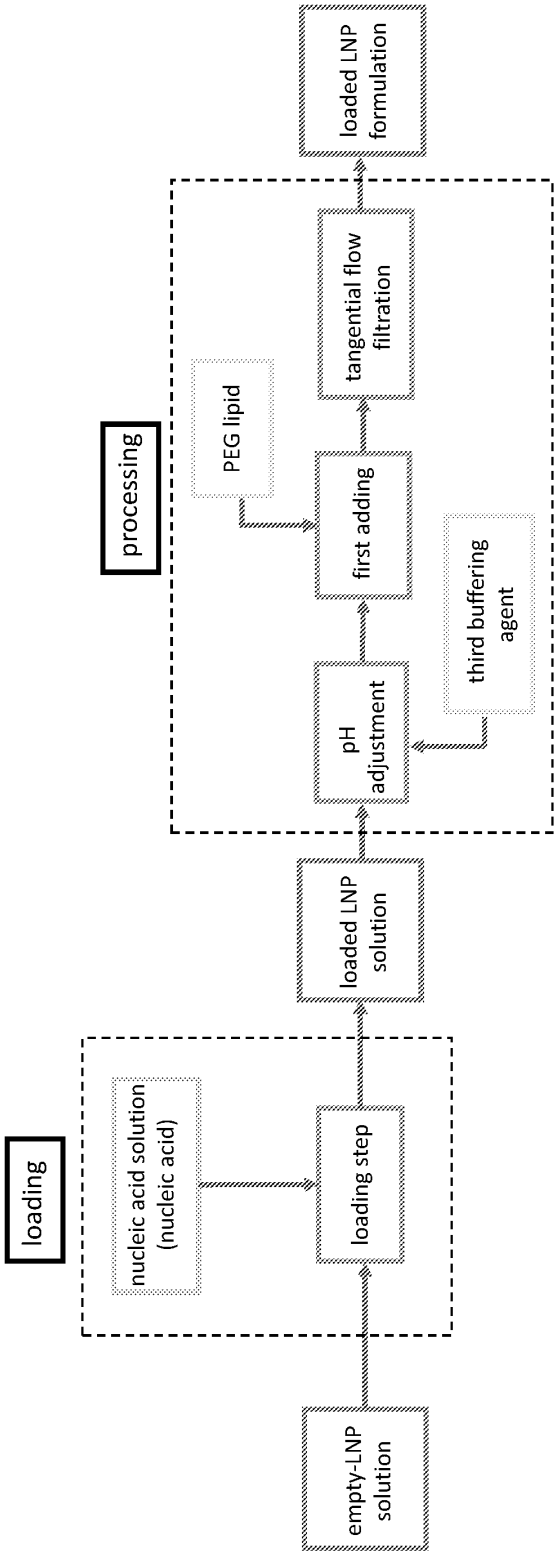

loading
nucleic acid solution (nucleic acid)
loading step
empty-LNP solution
loaded LNP solution
processing
PEG lipid
first adding
pH adjustment
third buffering agent
tangential flow filtration
loaded LNP formulation

Fig. 7

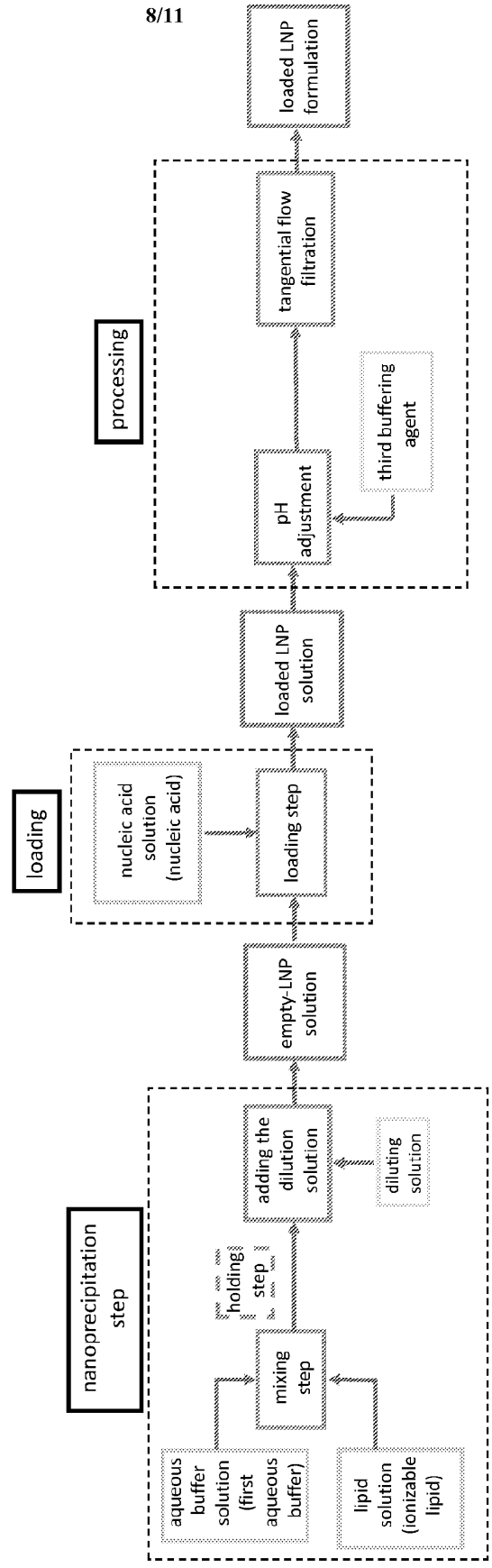

nanoprecipitation step
aqueous buffer solution (first aqueous buffer)
lipid solution (ionizable lipid)
mixing step
holding step
adding the dilution solution
diluting solution
empty-LNP solution
loading
nucleic acid solution (nucleic acid)
loading step
loaded LNP solution
processing
pH adjustment
third buffering agent
tangential flow filtration
loaded LNP formulation

Fig. 8

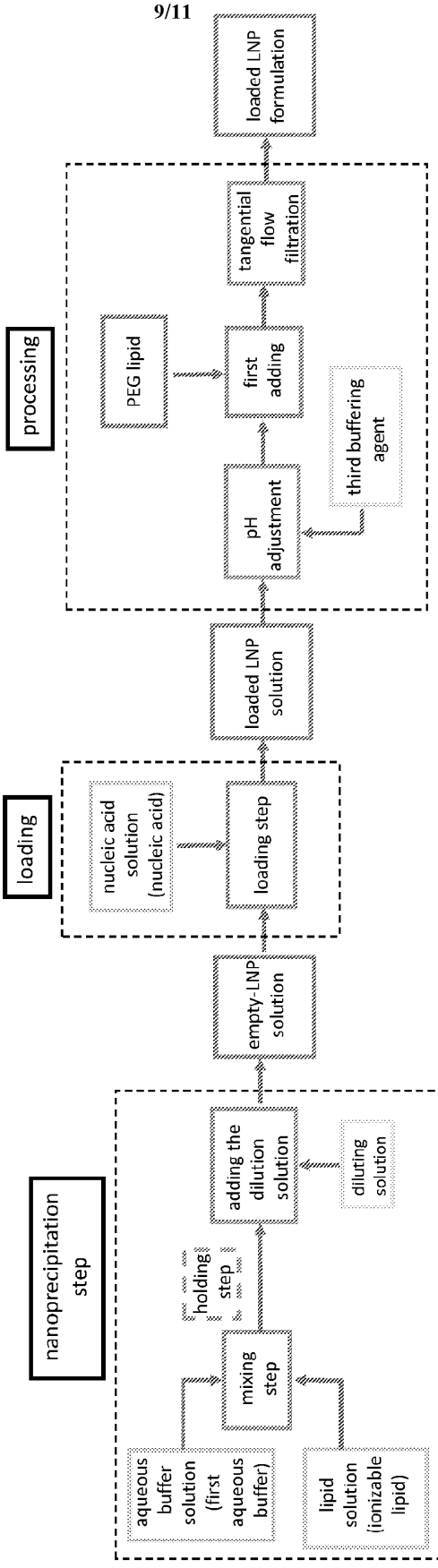

nanoprecipitation step
aqueous buffer solution (first aqueous buffer)
lipid solution (ionizable lipid)
mixing step
holding step
adding the dilution solution
diluting solution
empty-LNP solution
loading
nucleic acid solution (nucleic acid)
loading step
loaded LNP solution
processing
pH adjustment
third buffering agent
first adding
PEG lipid
tangential flow filtration
loaded LNP formulation

Fig. 9

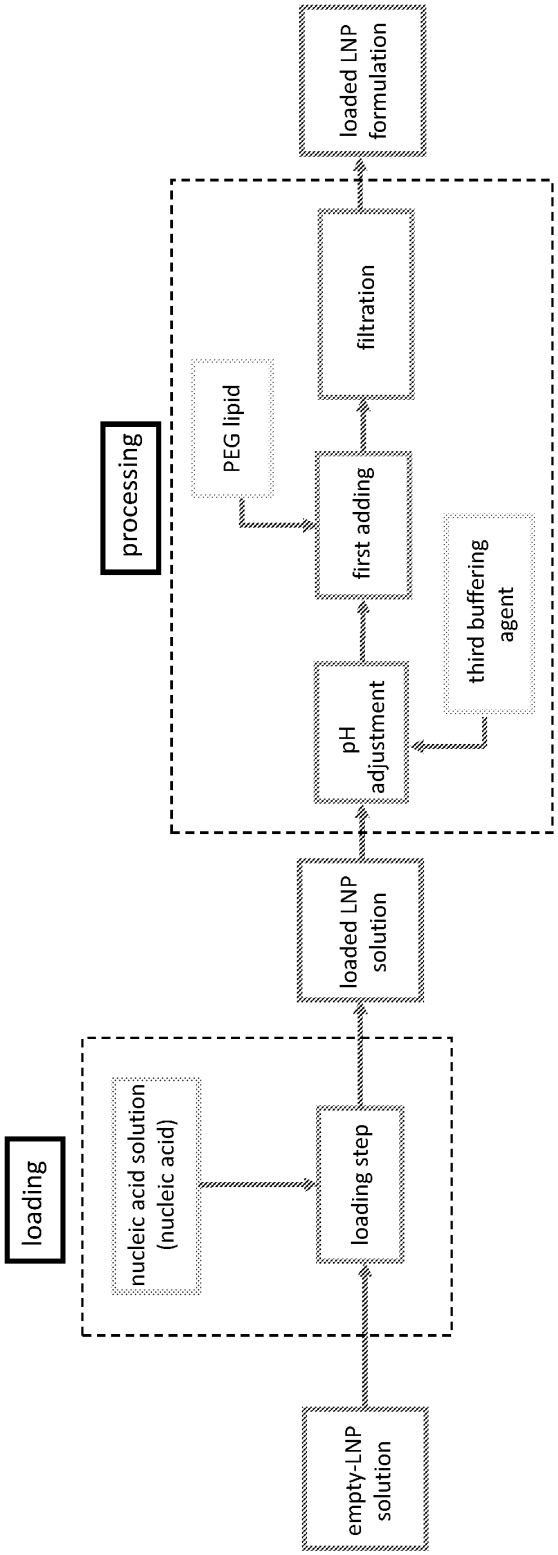

loaded LNP formulation
processing
filtration
PEG lipid
first adding
third buffering agent
pH adjustment
loaded LNP solution
loading
nucleic acid solution (nucleic acid)
loading step
empty-LNP solution

Fig. 10

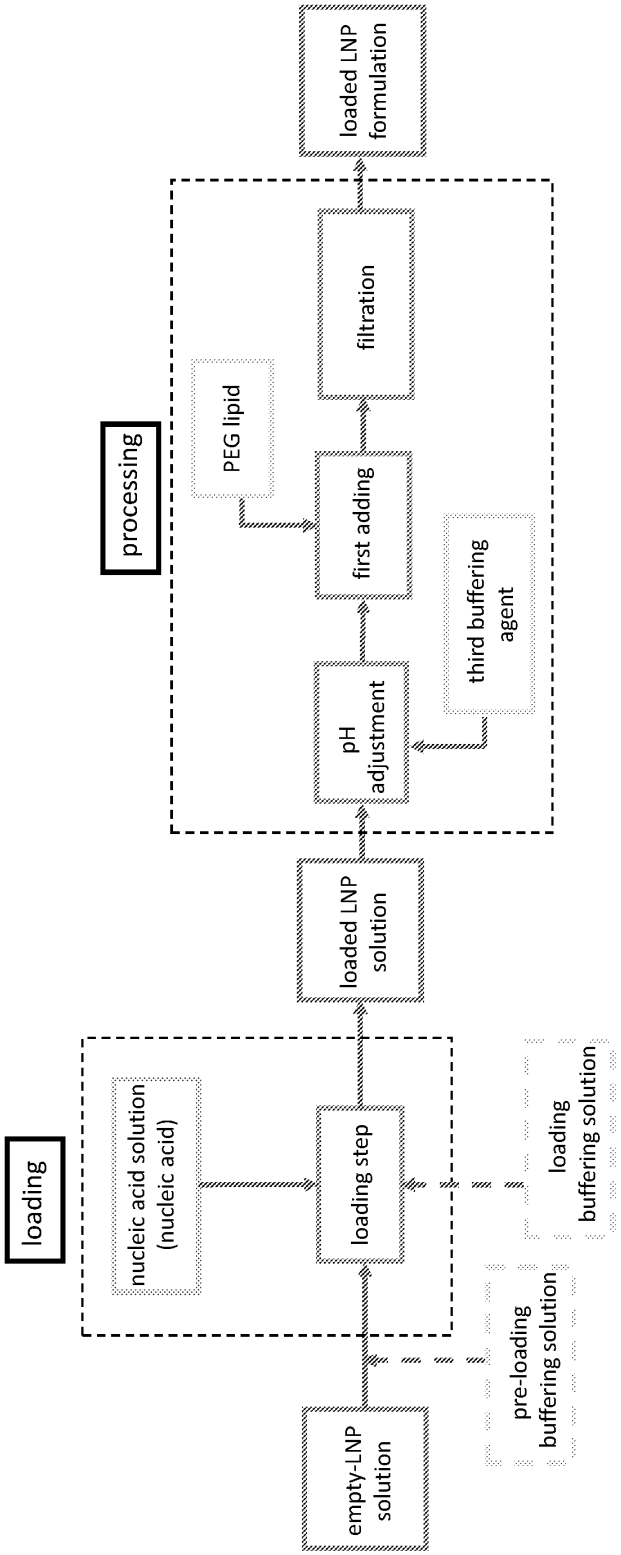

loaded LNP formulation
processing
filtration
PEG lipid
first adding
third buffering agent
pH adjustment
loaded LNP solution
loading
nucleic acid solution (nucleic acid)
loading step
loading buffering solution
pre-loading buffering solution
empty-LNP solution

Fig. 11