CLAIMS

1. A method for quantifying the abundances of target proteins in a biological sample, comprising:

capturing the target proteins by exposing the biological sample to a plurality of aptamers each configured to bind to a specific protein;

isolating the aptamers that captured one of the target proteins in an aptamer-containing eluate;

forming a plurality of tri-molecular complexes by exposing the aptamers in the eluate to a plurality of capture probes each configured to hybridize to a particular aptamer, each tri-molecular complex including:

one of the aptamers from the eluate,

a first capture probe including a portion hybridized to a first portion of the aptamer, and

a second capture probe including a portion hybridized to a second portion of the aptamer, a DNA primer region, and an aptamer ID sequence corresponding to the aptamer;

separating the tri-molecular complexes from capture probes not bound to aptamers;

dissociating the capture probes in the tri-molecular complexes from the corresponding aptamers;

amplifying the aptamer ID sequences of the dissociated second capture probes;

sequencing the amplified aptamer ID sequences of the dissociated second capture probes via next-generation sequencing; and

based on data obtained by sequencing the aptamer ID sequences, determining the abundances of the target proteins in the biological sample.

2. The method of claim 1, wherein the aptamers have a rate of protein-aptamer dissociation $t_{1/2}$ between 30 and 240 minutes.

3. The method of claim 1, further comprising dividing the aptamer-containing eluate into two or more groups prior to forming the tri-molecular complexes, and wherein the

aptamers in each aptamer-containing eluate group are exposed to a different set of capture probes.

4. The method of claim 1, further comprising dividing the dissociated capture probes into a plurality of aliquots prior to amplifying the aptamer ID sequences of the dissociated second capture probes, and wherein amplifying the aptamer ID sequences includes amplifying a different subset of aptamer ID sequences in each aliquot.

5. The method of claim 4, further comprising diluting at least one of the aliquots before amplifying the aptamer ID sequences of the dissociated second capture probes.

6. The method of claim 4, further comprising adding a quantitative spike reporter to each aliquot before amplifying the aptamer ID sequences of the dissociated second capture probes.

7. The method of claim 6, further comprising recombining the aliquots prior to sequencing the amplified aptamer ID sequences of the dissociated second capture probes.

8. A method for quantifying the abundances of two or more species of target proteins in a biological sample, comprising:

capturing the target proteins by exposing the biological sample to a plurality of aptamers each configured to capture a specific protein;

forming an aptamer-containing eluate by isolating the aptamers that captured one of the target proteins in the biological sample;

forming a plurality of tri-molecular complexes, each including:

a particular aptamer present in the aptamer-containing eluate,

a first probe hybridized to a corresponding first portion of the particular aptamer, and

a second probe including a portion hybridized to a corresponding second portion of the particular aptamer, at least one DNA primer region, and an aptamer ID sequence corresponding to the particular aptamer;

amplifying the aptamer ID sequences of the second probes;

sequencing the amplified aptamer ID sequences of the second probes; and

based on the sequenced aptamer ID sequences, quantifying the abundances of the target proteins.

9. The method of claim 8, wherein the aptamers have a rate of protein-aptamer dissociation $t_{1/2}$ between 30 and 240 minutes.

10. The method of claim 8, further comprising dividing the aptamer-containing eluate into two or more dilution groups prior to forming the tri-molecular complexes, and wherein each dilution group contains a distinct set of capture probes.

11. The method of claim 8, further comprising dividing the capture probes into a plurality of aliquots prior to amplifying the aptamer ID sequences of the second probes, wherein at least one of the aliquots is diluted, and wherein amplifying the aptamer ID sequences of the second probes includes amplifying a different subset of aptamer ID sequences in each aliquot.

12. The method of claim 11, further comprising adding a quantitative spike reporter to each aliquot before amplifying the aptamer ID sequences of the second probes.

13. The method of claim 12, further comprising recombining the aliquots prior to sequencing the amplified aptamer ID sequences of the second probes.

14. The method of claim 8, wherein sequencing the amplified aptamer ID sequences of the second probes is accomplished via next generation sequencing.

15. A method for detecting a target protein in a biological sample, comprising:

capturing the target protein with an aptamer by combining the biological sample with a plurality of aptamers each configured to capture a specific protein;

forming a tri-molecular complex including:

the aptamer that captured the target protein,

a first probe including a portion hybridized to a corresponding first portion of the aptamer that captured the target protein, and

a second probe including a portion hybridized to a corresponding second portion of the aptamer that captured the target protein, at least one DNA primer region, and an aptamer ID sequence corresponding to the aptamer that captured the target protein;

amplifying the aptamer ID sequence of the second probe; and

sequencing the amplified aptamer ID sequence of the second probe to identify the aptamer ID sequence of the second probe, thereby identifying the aptamer that captured the target protein and identifying the target protein.

16. The method of claim 15, further comprising forming the first and second probes by determining a target region on the aptamer, and then determining a boundary for dividing a complement of the target region into the first and second probes.

17. The method of claim 16, wherein determining the boundary is based on achieving desired melting temperatures for the hybridized portions of the first and second probes.

18. The method of claim 17, further comprising determining the melting temperature of the complement of the target region computationally, and then stepping through boundary changes between the hybridized portions of the first and second probes until the desired melting temperatures of the hybridized portions are achieved.

19. The method of claim 17, wherein sequencing the amplified aptamer ID sequence of the second probe is accomplished via next generation sequencing.

20. The method of claim 15, further comprising dissociating the second probe from the aptamer before amplifying the aptamer ID sequence of the second probe.

21. The method of claim 1, wherein the aptamers have chemically modified nucleotides.

22. The method of claim 8, wherein the aptamers have chemically modified nucleotides.