CLAIMS

What is claimed is:

1. A method for in situ genomic and transcriptomic assessment of target nucleic acids present in a biological sample comprising the steps of:

a) treating the biological sample with a small molecule linker comprising a chemical reactive group capable of covalently binding at least one target nucleic acid and a chemical group that can be incorporated into the a swellable material;

b) permeating the biological sample with a composition comprising precursors of a swellable material;

c) initiating polymerization of the precursors to form a swellable material, wherein the small molecule linker is bound to the at least one target nucleic acid in the biological sample and to the swellable material;

d). subjecting the biological sample to a physical disruption method;

e). swelling the swellable material to form an expanded biological sample;

f). providing at least one oligonucleotide complementary to the at least one target nucleic acid, wherein the at least one oligonucleotide hybridizes to the at least one target nucleic acid; and

g). genomically or transcriptomically assessing the expanded biological sample.

2. The method according to claim 1, wherein the small molecule linker is labeled.

3. The method according to claim 2, wherein the expanded biological sample expresses one or more labeled target nucleic acids.

4. The method according to claim 1, wherein the at least one oligonucleotide is labeled.

5. The method according to claim 1, wherein the at least one target nucleic acid is anchored to the swellable material.

6. The method according to claim 1, wherein the physical disruption method is an enzymatic digestion.

7. The method according to claim 1, wherein the target nucleic acids are DNA and/or RNA.

8. The method according to claim 1, further comprising the additional step of buffering the expanded sample.

9. The method according to claim 8, further comprising the additional step of re-embedding the buffered expanded biological sample in a non-swellable material.

10. The method according to claim 9, further comprising the step of removing the at least one oligonucleotide complementary to the at least one target nucleic acid.

11. The method according to claim 10, wherein the steps of providing at least one oligonucleotide, genomically or transcriptomically assessing the expanded biological sample and removing the at least one oligonucleotide are repeated so as to allow serial or sequential genomic or transcriptomic assessments of the expanded biological sample.

12. The method of claim 10, wherein removing the at least one oligonucleotide which is hybridized to the at least one target nucleic acid comprises formamide and high temperatures.

13. The method of claim 10, wherein removing the at least one oligonucleotide which is hybridized to the at least one target nucleic acid comprises endonucleases that specifically digest the at least one oligonucleotide.