CLAIMS

1. A method for synthesizing an RNA molecule of a given sequence, comprising the following steps:

   a) determining the fraction (1) for each of the four nucleotides G, A, C and U in said RNA molecule, and

   b) synthesizing said RNA molecule by *in vitro* transcription in a sequence-optimized reaction mix, wherein said sequence-optimized reaction mix comprises the four ribonucleoside triphosphates (NTPs) GTP, ATP, CTP and UTP, wherein the fraction (2) of each of the four ribonucleoside triphosphates in the sequence-optimized reaction mix corresponds to the fraction (1) of the respective nucleotide in said RNA molecule, a buffer, a DNA template, and an RNA polymerase.

2. The method of claim 1, wherein step b) comprises the steps of

   b1) preparing a sequence-optimized ribonucleoside triphosphate (NTP) mix comprising the four ribonucleoside triphosphates (NTPs) GTP, ATP, CTP and UTP, wherein the fraction (2) of each of the four ribonucleoside triphosphates in the sequence-optimized ribonucleoside triphosphate (NTP) mix corresponds to the fraction (1) of the respective nucleotide in said RNA molecule, and

   b2) synthesizing said RNA molecule by *in vitro* transcription in the sequence-optimized reaction mix comprising the NTP mix of step (b1), a buffer, a DNA template, and an RNA polymerase.

3. The method of claim 1 or 2, wherein before the start of the *in vitro* transcription a start nucleotide is added to the sequence-optimized reaction mix which corresponds to the first nucleotide of said RNA molecule.

4. The method of claim 3, wherein said start nucleotide is a nucleoside monophosphate, a nucleoside diphosphate, a nucleoside triphosphate or a di-nucleoside triphosphate or a cap analog.

5. The method of any of claims 3 or 4, wherein said start nucleotide is added in excess compared to the fraction of that nucleotide in said RNA molecule which is found at the first position of said RNA molecule.

6. The method of any of claims 1 to 5
wherein for the nucleotides which do not correspond to the first nucleotide of the RNA molecule fraction (1) and fraction (2) differ by at most 10 %.

7. The method of any of claims 1 to 6, wherein a part or all of at least one ribonucleoside triphosphate is replaced by a modified nucleoside triphosphate, wherein said modified nucleoside triphosphate is preferably selected from the group consisting of pseudouridine-5'-triphosphate, 1-methylpseudouridine-5'-triphosphate, 2-thiouridine-5'-triphosphate, 4-thiouridine-5'-triphosphate and 5-methylcytidine-5'-triphosphate.

8. The method of any of claims 1 to 7, wherein in the course of the *in vitro* transcription the sequence-optimized reaction mix is supplemented with the sequence-optimized ribonucleoside triphosphate (NTP) mix as defined in claim 2 b1).

9. The method of any of claims 1 to 8, wherein said RNA molecule is selected from the group consisting of non-coding and coding RNA molecules, preferably an mRNA.

10. The method of any of claims 1 to 9, wherein said RNA molecule is longer than 100 nucleotides, and/or wherein said synthesizing of an RNA molecule of a given sequence is performed as a large scale synthesis and/or wherein the NTP counter ion is tris(hydroxymethyl)-aminomethane (Tris).

11. The method of any of claims 1 to 10, wherein the synthesizing of said RNA molecule by *in vitro* transcription is followed by separating and quantifying the unincorporated NTPs.

12. The method of any of claims 1 to 11, wherein the synthesizing of said RNA molecule by *in vitro* transcription is carried out in a bioreactor (1), wherein said bioreactor (1) preferably comprises a DNA template immobilized on a solid support.

13. The method of claim 12, wherein said bioreactor (1) comprises a filtration membrane (21) for separating nucleotides from the sequence-optimized reaction mix, wherein said filtration membrane (21) is preferably selected from the group of regenerated cellulose, modified cellulose, polysulfone (PSU), polyacrylonitrile (PAN), polymethylmethacrylate (PMMA), polyvinyl alcohol (PVA) and polyarylethersulfone (PAES).

14. The method of claim 13, wherein said filtration membrane (21) has a molecular weight cut-off in a range of approximately 10 to 50 kDa.

15. The method of any of claims 12 to 14, wherein said bioreactor (1) comprises a sensor unit (41) for the real-time measurement of the nucleotide concentration during the reaction, wherein said sensor unit (41) preferably measures the nucleotide concentration by photometric analysis.

16. The method of any of claims 12 to 15, wherein said bioreactor comprises a control module (4) which controls the addition of the sequence-optimized ribonucleoside triphosphate (NTP) mix as defined in claim 2 b1) and/or wherein said bioreactor (1)

comprises an actuator (43) which adds the sequence-optimized ribonucleoside triphosphate (NTP) mix as defined in claim 2 b1), and/or wherein said bioreactor (1) comprises a resin to capture the RNA molecules and to separate the RNA molecules from the other components of the transcription reaction mix and/or wherein said bioreactor (1) operates in a semi-batch mode or in a continuous mode.

17. The method of any of claims 12 to 16, wherein said bioreactor (1) comprises at least one ion-selective electrode, wherein the at least one ion-selective electrode is preferably used for measuring the concentration of one or more types of ions in a liquid comprised in at least one compartment of the bioreactor (1), wherein the ion is preferably selected from the group consisting of H^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^- and PO_4^{3-}.