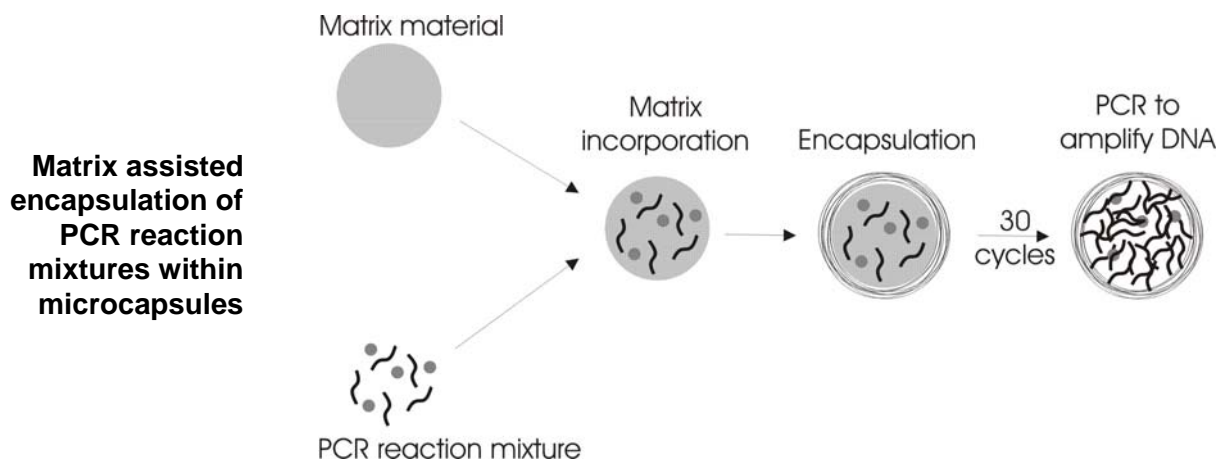


Microcapsule - PCR: High throughput PCR for screening, genomic libraries and sequencing

PCR? The polymerase chain reaction (PCR) is an important method in molecular biology with various applications in clinical research, diagnostics and biotechnology. Millions of PCRs are carried out every day in laboratories world wide for research purpose or to identify pathogenic bacteria or viruses.

Today's technology Today, PCR reactions are carried out in reaction tubes, micro titer plates or glass capillaries. The reaction volume is usually ~50 μ l and can be as low as 10 μ l by using the most advanced instruments. The parallelism of PCR is restricted to about 48 reactions by using tubes and 96 to 1539 reactions per run by using high-density microtiter plates. However, these numbers are still too small to perform large screening projects, e.g. in pharmacological research in appropriate time. In current PCR techniques, individual PCR reactions are separated by using reaction tubes, capillaries or wells made from plastic ware or glass. To perform a higher number of reactions in parallel, the integration density must be increased and the reaction volume must be decreased. This has limited chance to succeed by using the current technology.

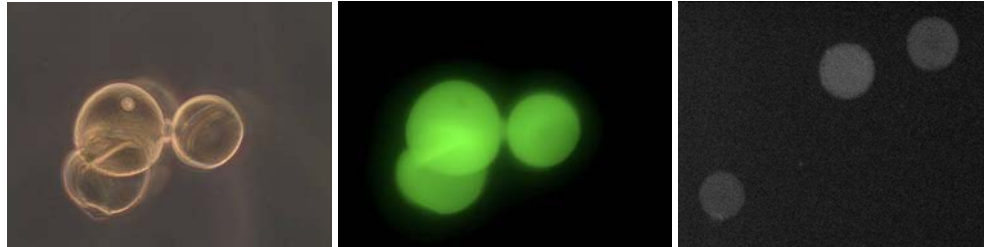
New approaches and opportunities We developed a totally new approach to overcome those limitations. The new technology of "Microcapsule-PCR" is under development in our laboratories. Recently, a world patent was filed on this invention that allows performing millions of PCR reactions in parallel in a single reaction tube.



"Microcapsule-PCR" is based on the encapsulation of a PCR reaction mixture into microcapsules of ~50 μ m in diameter by using our technique of "matrix assisted encapsulation". The capsules create a compartment to separate individual PCR reactions from each other. A very high number of individual PCR reactions can be carried out in a single reaction tube. We are able to control the permeability of the microcapsules. Capsules are not permeable for the PCR product but permeable for reactants (dNTPs). This allows that reactants can be feed from the outside and PCR product accumulates in the interior of capsules. By using fluorescent labeled building blocks (dNTPs) the resulting PCR product is fluorescent labeled and such capsules can be easily detected and isolated due to their fluorescent intensity.

Applications “Microcapsule-PCR” allows increasing the throughput dramatically. The technology can be applied for screening of nucleic acids (Virus/bacteria detection) and for diagnostics. A very promising application is the production of genomic or cDNA libraries in a much faster and simpler way. Such libraries are important for research and to manufacture DNA-microarrays. We also have a new approach to sequence a genome, by using our library construction method, much faster than possible with current methods.

Microcapsules encapsulating a PCR reaction mixture



The images above show microcapsules encapsulating a PCR mixture. Left: morphology of capsules. Middle: Fluorescent stained capsule material. Left: Fluorescent stained PCR product in interior of capsules.

Project status The basic principle of matrix assisted encapsulation of PCR reaction mixtures and “Microcapsule-PCR” is established in our laboratory. A patent application with world wide coverage is filed on the technology. This patent claims the basic technology and its sequence and genomic library construction applications. Those applications will be explored with collaboration partners from different disciplines.

Our strength At NUS we have a perfect environment to carry out “Microcapsule-PCR” related research. Our research facilities at our “Bioengineering Corridor” are fully equipped for molecular biology research and microscopic and physical studies. Combined with the expertise of our faculty and research staff we position ourselves very competitive to develop this invention into a powerful tool with various applications in molecular biology and medical diagnostics.

Industrial collaboration partner wanted We are looking for academic and industrial partners with ambitions in medical diagnostics/sequencing and for a partner in the clinical setting to complement our strength towards medical applications of the technology.



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