



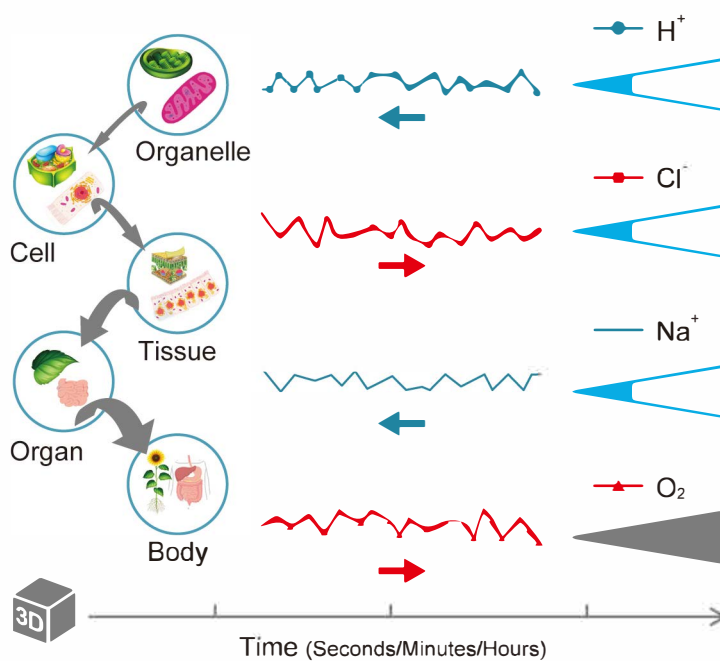
Life  Environment

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NMT & Its Applications

Non-invasive Micro-test Technology in Life Sciences



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Abstract

Life is an irreversible dynamic equilibrium in which ions and molecules are constantly exchanging between its internal and external environments. NMT: Non-invasive Micro-test Technology can detect this dynamic process by measuring concentration gradients, namely ionic/molecular fluxes, in multi-dimensions in real time and in situ with live samples. NMT has a super sensitivity capable of detecting Ca^{2+} fluxes of a single cell, e.g. a pollen grain, which has been making it an invaluable tool for scientists in many scientific fields. In this life science version, applications from biomedical research to plant and crop sciences, animal science, environmental science, microbiology to marine biology et al. have been covered. Brief NMT history and some new features integrated with current AI capabilities as well as NMT for higher education are also introduced hoping to inspire young scientists to explore this exciting area in the future. Standardization in terms of SOPs stemmed from pioneer NMT scientists, commercialization and industrialization of NMT are also introduced as references for both ambitious bio-entrepreneurs and new people who just came across this technology. The promising imOmics and its related projects, such as Bio-imOmics Project are explained with intention to guide people to fully appreciate the integration capabilities of NMT in the upcoming multi-omics age.



Keywords

NMT, Non-invasive Micro-test Technology, Ions, Molecules, Fluxes, Sensors, Microelectrodes, Transmembrane transport, Microenvironment, Life Sciences, imOmics, BiP, Bio-imOmics Project

Contents

Abstract	2
Keywords	2
1 Introduction	6
2 NMT: Non-invasive Micro-test Technology	7
2.1 PRINCIPLES & FEATURES	7
2.1.1 <i>Two-points measurement scheme</i>	7
2.1.2 <i>Fluxes & voltage differences</i>	8
2.1.3 <i>Artificial ionic/molecular source tests & dynamic calibrations</i>	9
2.1.4 <i>Physical & chemical spaces</i>	9
2.1.5 <i>1D, 2D, 3D and 6D measurements</i>	10
2.1.6 <i>High-throughput NMT in AI Era</i>	12
2.1.7 <i>Gradraw® & NMT visualization</i>	13
2.2 LIMITATIONS OF NMT	13
2.2.1 <i>NMT Micro-sensors</i>	13
2.2.2 <i>Temporal resolution</i>	14
2.2.3 <i>Spatial Resolution</i>	14
2.3 COMPARATIVE ADVANTAGES WITH OTHER TECHNIQUES	14
2.3.1 <i>NMT vs. Micro-electrodes</i>	14
2.3.2 <i>NMT vs. Patch Clamp</i>	15
2.3.3 <i>NMT vs. Fluorescence Microscopy</i>	17
2.3.4 <i>NMT vs. Radioactive Labeling, NMR, Gas Chromatography, Cyclic Voltammetry and Nano SIMS</i>	17
3 NMT in biological and biomedical research	19
3.1 HUMAN PATHOLOGY	19
3.1.1 <i>Tumor</i>	19
3.1.1.1 <i>Glioma</i>	19
3.1.1.2 <i>Oral squamous cell carcinoma</i>	19
3.1.1.3 <i>Anti-cancer Drug Resistance</i>	19
3.1.2 <i>Diabetes</i>	19
3.1.2.1 <i>Dapagliflozin & O₂</i>	19
3.1.2.2 <i>Ca²⁺ flux & insulin secretion type-II diabetes</i>	19
3.1.2.3 <i>Ca²⁺ flux & insulin secretion type-I diabetes</i>	20
3.1.3 <i>Edema</i>	20
3.1.3.1 <i>Bumetanide side effects</i>	20
3.1.4 <i>Toxicology</i>	20
3.1.4.1 <i>Nanomaterials & environmental toxicity evaluation</i>	20
3.1.4.2 <i>Chitin & environmental toxicity evaluation</i>	20
3.2 HUMAN PHYSIOLOGY	20
3.2.1 <i>Gastroenterology</i>	20
3.2.1.1 <i>Entacapone side effects</i>	20
3.2.1.2 <i>Emodin & Cl⁻ secretion</i>	20
3.2.2 <i>Reproductive medicine</i>	21
3.2.2.1 <i>Apoptosis & K⁺ efflux</i>	21
3.2.2.2 <i>Oocyte viability and Ca²⁺/Na⁺ exchanger</i>	21
3.3 NEUROBIOLOGY	21
3.3.1 <i>Alzheimer & Ca²⁺</i>	21
3.3.2 <i>Alzheimer & K⁺/Ca²⁺</i>	21
3.3.3 <i>Alzheimer & Cu²⁺</i>	22
3.4 OTOLARYNGOLOGY	22
3.5 OPHTHALMOLOGY	22
3.5.1 <i>Myopia & K⁺ homeostasis</i>	22

3.5.2 Retina & H ⁺ flux.....	23
3.6 REGENERATIVE MEDICINE.....	23
3.7 PRECISION PERSONALIZED MEDICINE	23
3.8 TRADITIONAL CHINESE MEDICINE PHARMACOLOGY	23
3.8.1 Pharmacology of TCM	23
3.8.2 Acupuncture mechanism & IMH.....	23
3.9 PHARMACOLOGY.....	23
3.10 PHARMACY	24
3.11 SPORTS MEDICINE.....	24
3.11.1 Muscle injuries & Ca ²⁺ homeostasis	24
3.11.2 Muscle energy & O ₂ flux	25
3.11.3 Muscle Tension & Ca ²⁺ Flux.....	25
3.12 ENTOMOLOGY	25
3.12.1 Two Distinct Ion-regulation Mechanisms.....	25
3.12.2 Insect hormone & ionic homeostasis	25
3.13 ANIMAL PHYSIOLOGY AND BEHAVIORS	25
3.13.1 Muscle contraction & Ca ²⁺ Source.....	25
3.13.2 Ions acquisition in embryos.....	26
3.14 PLANT PHYSIOLOGY AND BIOCHEMISTRY	26
3.14.1 Resistance physiology	26
3.14.1.1 Salt stress	26
3.14.1.1.1 GORK/NSCC & K ⁺ preservation	26
3.14.1.1.2 Proton pump H ⁺ -ATPase & H ⁺	26
3.14.1.1.3 Na ⁺ , K ⁺ , H ⁺ & Ca ²⁺	26
3.14.1.1.4 PePLD/SOS2–SOS1/ PI4P/PI/ GmSALT3 & Na ⁺ /K ⁺ homeostasis	27
3.14.1.2 Temperature stress	27
3.14.1.2.1 Low temperature & Ca ²⁺ influxes in COLD1	27
3.14.1.2.2 Low Temperature & LSI1/ OsCNGC9 Salt Tolerance Genes	27
3.14.1.2.3 High Temperature & TT2 (THEROMOTOLERANCE 2).....	27
3.14.1.2.4 High temperature & HTS1/KAR.....	27
3.14.1.3 Heavy metal stress.....	27
3.14.1.3.1 Cd ²⁺ /Cu ²⁺ /Pb ²⁺ influxes detected.....	27
3.14.1.3.2 Mg ²⁺ , K ⁺ , Ca ²⁺ & heavy metal stress.....	27
3.14.1.3.3 H ⁺ , O ₂ & nutrient absorption and redox potential	27
3.14.1.3.4 Cd ²⁺ detoxification by NH ₄ ⁺	27
3.14.1.3.5 Cd ²⁺ absorption & Ca ²⁺ channels.....	28
3.14.1.3.6 OsHIPP9/BcHIPP16 & Cu ²⁺ , Cd ²⁺ absorptions.....	28
3.14.1.3.7 HvNAT2-OX & Cd ²⁺ absorption	28
3.14.1.4 Water stress	28
3.14.1.4.1 H ⁺ , K ⁺ , Ca ²⁺ , H ₂ O ₂ & water stress.....	29
3.14.1.4.2 ABA, IAA & drought resistance	29
3.14.1.4.3 Stomata closure & H ₂ S , SAL1-PAP signaling pathway	29
3.14.1.4.4 Stomatal closure, PM H ⁺ -ATPases & ABA.....	29
3.14.1.5 Plant immunity.....	29
3.14.1.5.1 Ca ²⁺ & Herbivory	29
3.14.1.5.2 K ⁺ & Plant immunity	29
3.14.1.5.3 Ca ²⁺ & Plant immunity	29
3.14.1.5.4 eATP & Stress tolerance.....	29
3.14.2 Plant hormones and growth and development.....	30
3.14.2.1 ABA & Leaf Senescence	30
3.14.2.2 IAA & H ⁺ , K ⁺ , Ca ²⁺	30
3.14.2.3 Ca ²⁺ & Pollen tube growth	30
3.14.3 Plant microbial interactions	30
3.14.3.1 EMF & Plant nutrients absorption.....	31
3.14.3.2 PGPR & Plant tolerance.....	31
3.14.4 Plant nutrition	31

3.14.4.1	Temporal and spatial factors	31
3.14.4.2	The Acidity and alkalinity	31
3.14.4.3	NH ₄ ⁺ Toxicity.....	32
3.14.4.4	A Rhythmic pattern	32
3.15	ENVIRONMENTAL MICROBIOLOGY	32
3.16	BIOLOGICAL OCEANOGRAPHY AND MARINE LIVING RESOURCES.....	32
3.16.1	<i>Seagrass ecosystem & NH₄⁺ source</i>	32
3.16.2	<i>Salinity & Heavy metal tolerance</i>	32
3.17	APPLICATIONS IN BIOSAFETY.....	33
3.18	APPLICATIONS IN SPACE BIOLOGY.....	33
3.19	SUMMARY	33
4	History & prospects	34
4.1	HISTORY	34
4.1.1	<i>Origin</i>	34
4.1.2	<i>NMT for higher education</i>	34
4.1.3	<i>NMT in China & the World</i>	34
4.1.4	<i>Zhongguancun Xuyue NMT Industrial Alliance</i>	35
4.1.5	<i>NMT standardizations & SOP</i>	35
4.1.6	<i>NISC: NMT International Standard Committee</i>	35
4.1.7	<i>Chinese National Group Standards Publication Platform</i>	36
4.1.8	<i>NMT hardware/software/services certifications</i>	36
4.2	PROSPECTS	36
4.2.1	<i>imOmics & BiP</i>	36
4.2.2	<i>NMT Industrializations</i>	36
4.2.3	<i>NMT International Alliance: NMTia</i>	37
5	Conclusions.....	38
	References.....	39
	Supplementary data.....	50
	Tables	50
	TABLE 1. LIST OF COMMERCIALY AVAILABLE NMT-MICROSENSORS AND SUPPORTING REFERENCES	50
	TABLE 2. NMT COMPARED TO OTHER ION/MOLECULE DETECTION TECHNIQUES	51
	TABLE 3. SUMMARY OF SAMPLES TESTED BY NMT	52
	TABLE 4. LIST OF CATEGORIZED REFERENCES BY APPLICATION FIELDS.....	54
	TABLE 5. SUMMARY OF NMT RELATED TEXTBOOKS AND BOOK CHAPTERS	74
	TABLE 6. SUMMARY OF STANDARD OPERATION PROCEDURE (SOP) APPROVED BY NISC OF NMTia	76
	TABLE 7. SUMMARY OF PRODUCT & SERVICE ASSURANCE & CERTIFICATES APPROVED BY NMTia	77
	TABLE 8. NMT VIDEOS OF TUTORIALS, LECTURES, TECHNICAL PRESENTATIONS ET AL.....	78

1 Introduction

Ions and molecules are not only the basic particles that make up all things in the world, but also an important medium for information exchange and energy conversion between living and non-living substances and their external environments. From Ion and Molecule Homeostasis (IMH) perspective, it is essential to study ionic/molecular activities in life sciences¹⁻⁹. Diseases of humans, animals, crops, insects and microbes et al. are usually accompanied by abnormal IMHs. Excessive H^+ accumulations, for instance, is the result from lactate formation even in the presence of O_2 in tumor cells demonstrated by Nobel laureate Warburg nearly a century ago¹⁰⁻¹⁴. It is also well known that a plant will not grow properly if the supply of NH_4^+ , NO_3^- , PO_4^{3-} , K^+ among other ions/molecules are out of balance¹⁵⁻¹⁸.

However, it has been a daunting challenge for biologists to fully comprehend the IMHs due to:

a) ionic and molecular information related to IMH have to be collected with live samples in order to make reliable and practical sense of those data;

b) multiple ions/molecules are preferably measured simultaneously in order to construct the relationship network among relevant ion(s)/molecule(s) to a specific physiological process;

c) ionic/molecular data in different levels, i.e. cell, tissue to organ, has to be collected due to the increasing evidence that there are dramatic differences of ionic/molecular transmembrane activities from cellular to tissue and/or organ levels;

d) since biological materials are 3-dimensional per se, 1D or 2D form of data is no longer accurate enough to reflect the biological real 3D world¹⁹⁻²³.

In the last 20+ years, Non-invasive Micro-test Technology (NMT) has been proved to be able to tackle these challenges mentioned above^{9,24}.



2 NMT: Non-invasive Micro-test Technology

2.1 Principles & features

2.1.1 Two-points measurement scheme

Ionic/molecular fluxes will be detectable when ions/molecules move from higher concentrations to lower concentrations. The concentration differences will then result in ionic/molecular gradients (**Figure 1**). In the scenarios of live biological samples, transmembrane activities of ions/molecules will result in ionic/molecular gradients via their effluxes and/or influxes²⁵.

In order to measure these ions/molecules selectively or specifically in a quantitative way, various sensors made from different materials, such as glass, optical fiber, platinum-iridium alloy, nanoparticles et al., have been developed (**Table 1**).

These sensors' fabrications are based on different theories/mechanisms, such as ionophore special characteristics, enzymatic reactions, electrochemistry, fluorescent dyes etc.²⁶. Due to the special demands of temporal and spatial resolutions, conventional ionic/molecular sensors usually have to be modified to meet the requirements from NMT hardware configuration. Therefore, NMT ionic/molecular micro-sensors are designated to differentiate themselves from those traditional micro-sensors.

