**Title** From Files to Vials: A Framework for a Tissue-on-Chips Facility Aboard the International Space Station

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**Motivation and Aim**. In 2012 the National Research Counsil (NRC) called for a heightened awareness of the potential benefits of glycomics for medicine, materials science, and chemistry [1]. Much work has been accomplished in glycomics since this NRC report. The study of an extremely broad complement of monosaccharides, oligosaccharides, polysaccharides, and their derivatives has been investigated, and advances in the understanding of these biologic modifiers have been considerable. This white paper examines the applications of glycomic production aboard the ISS, in order to reap benefits in medicine, energy, materials science, and food production for consumers on Earth, as well as any Earth-orbiting satellite, including the Moon.

In 2015-16 NASA conducted the Twins Study, in which identical twins, Scott and Mark Kelly, were physiologically monitored for 240 days in order to ascertain what effect a low gravity Earth-orbiting environment would have on an ISS astronaut compared with a genetic counterpart on Earth. This was the closest evaluation comparable to a human physiological parity check that was possible at that time. The primary purpose of this proposal, From Files to Vials, is to examine the feasibility and practicality of an even closer parity check -- that between an ISS astronaut and her own tissue samples in a Tissue-on-Chips (ToC) **facility**, augmenting the current NCATS/NASA ToC experiment currently being conducted aboard the ISS.

A strategy for creating Systems-on-Chips (SoC) algorithms, i.e., the **Files**, will be developed so that viable and novel pharmaceuticals, nutraceuticals, biomechanical implants, and other biological modifiers, i.e., the **Vials**, can be produced aboard the ISS. It is expected that this experiment will be conducted ancillary to the current ISS facilities, and modularly integrate into the current NCATS/NASA ToC joint project.

**Action Plan.** The action plan should be flexible, and one which can provide measurable and sustainable incubators and accelerators for the biologics produced in the ISS ToC facility. Using modern quantum computing and neurocomputing algorithms [2], concurrent machine language, probabilistic dataflow architectures, SoC methods will be merged with just-in-time manufacturing and delivery methods to expand the current ISS ToC experiments. One benefit of such experiments would be to ascertain what effect, if any, non-Standard Temperature and Pressure (STP) environments have on glycolysis and glycan production.

A preliminary design template for the **Files** component shall include:

- Declaration blocks, or modules, to seamlessly transform from one design protocol., e.g., liposomal drug delivery systems, to another, e.g., artificial blood platelets;
- Software and firmware expression modules, perhaps written in Scala DSL or Systems Biology Markup Language (SBML), as are common to JSP (Java Servlet Pages), used for dynamic processing of glycans;

- Protocol and Method Modules, used for onboard repair, reprogramming, and recalibration of the glycolysis experiments and silicon chip and/or qubit substrates.
- Forward redirect logic gates and flip/flops, for ramping up or dampening down of glycolysis end products;
- Status call and response checkpoints, for realtime monitoring and control of the ToC facility;
- The ISS ToC network embedded variable scoping procedures and subroutines, for quality control and to ensure that the onboard pharmaceutical, nutraceutical, composites for onboard component replacements and bone implants, for example, as well as resins, and other biosynthetics;
- Anchor tags and latching firmware within the ISS ToC network to define *dynamic* glycolysis subprocessing boundaries within monosaccharide, polysaccharide, and oligosaccharide production;
- Directive modules, to override and/or reinforce the Declaration blocks during glycgogen production runtime;
- Exception handling logic gates on the ISS T0C network to catch runtime errors or out-of-bounds concentrations, catalysis rates, and other pharmacodynamics during production runtime;
- An application specific high level control language to model the process flow, balance loads among multiple glycan servers, model and monitor the intermediate biocompound concentrations, and be easily understood by humans. Such a control language shall be designed around well-established symbolic signaling algorithms, and follow as closely as possible international guidelines for natural language human-computer interfaces;
- Reusability features; as much as possible, ISS ToC modules shall be designed to incorporate on-chip capabilities for medicinal, energy, food, and biomaterial ligands. ToC networks shall be modular, and international biomedical standards shall be adhered to with respect to swap-out and add-on of chips and qubits.
- Action tags; logic redirection gates shall be seamlessly built into the ToC network, so that on-chip reactant, substrate, and catalysis ramp-up, as well as product off-load, can be easily and dynamically controlled;
- Both static, process-wide Include Action tags, as well as dynamic pre- and post-processing and subprocessing Include Directives, as are common in many machine markup languages, shall be utilized in order for fine-level control of the ToC glycan farm production;
- A Hibernate framework shall be engineered into the ToC network, to ensure ease of maintenance and upgrade of the ISS ToC network foundation;
- Standard or novel object-relational mapping techniques shall be incorporated into the ISS ToC hardware and software design, so that similar experiments and glycolysis

synthesis pathways can easily be merged into a standard ISS service protocol and interface for data translation;

- A transparent and systematic procedure for decompilation of all glycolysis pathways algorithms shall be provided as part of any ISS ToC module, for rapid and easy debugging and orderly ToC lifecycle shutdown.

Design specifications for the **Vials** component are more fluid. There currently exist several cutting-edge use cases [4,5,6,7,8,9,10,11,12] applicable for astrobiology. These glycolysis projects involve the production of medicines [4], vaccines [5], bioenergy boosters and biomagnetic implants [6], micro- and nanosurgical glycoprobes [7], glycol-microRNA genetic therapy interatomes [8], bovine milk production [9], metabolic syndrome studies [10], wound repair [11], and human toxicology[12].

All of these current, ongoing projects fulfill the call for action in the NRC 2012 Glycoscience Impact Study [1]. Yet all experiments are currently being conducted under standard pharmacokinetic and pharmacodynamic conditions, under standard pressure, temperature, Earth gravity, and Earth magnetic field constraints.

Fractional order processes for glycolysis experiments and glycan production aboard the ISS ToC facility shall thus include:

- A simulation facility to pre-test the production of astroglycolics using synthetic ground-based data [19];
- Regenerative medicine facilities, expanding on the current NASA Vascular Studies in Space Project [20]
- Novel agent-based metabolic, genetic, proteomic, and signal transduction tools for microRNA targeting of pathogens and neurological disorders, and discovery of new pharmacogenomics [17, 18];
- Novel onboard imaging tools, such as nuclear acoustic resonance imaging [21], to further the advances in the imaging of human physiological processes.

**Rollout.** This proposal, a Tissues-on-Chips factory aboard the ISS, is modest. It has potential benefits for all humankind, on Earth and in near Space, and potentially for Moon and Mars astronauts, too. Commercial, Agency, University, and secondary school experimenters and investigators would all play a role, from design to deployment. Additionally, just as there are United States land grant and sea grant colleges and universities, an international space grant college could be established. This international space grant college could be administered under the auspices of UNESCO, a European agency or laboratory, or an international philanthropic or business organization, such as Samsung or the HHMI. It would help to spur young researchers' curiosity in astrobiology and astrochemistry, and the economic benefits might be substantial.  Such a space grant college or university would foster diversity and promote the charter mission and vision of the ISS.

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