DEFENSE ADVANCED RESEARCH PROJECTS AGENCY (DARPA)
12.B Small Business Technology Transfer Program (STTR)
Proposal Submission Instructions

Introduction:

DARPA's mission is to prevent technological surprise for the United States and to create technological surprise for its adversaries. The DARPA SBIR and STTR Programs are designed to provide small, high-tech businesses and academic institutions the opportunity to propose radical, innovative, high-risk approaches to address existing and emerging national security threats; thereby supporting DARPA's overall strategy to bridge the gap between fundamental discoveries and the provision of new military capabilities.

The responsibility for implementing DARPA's Small Business Technology Transfer Program (STTR) Program rests with the Small Business Programs Office.

DEFENSE ADVANCED RESEARCH PROJECTS AGENCY
Attention: DIRO/SBPO
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(703) 526-4170
Home Page http://www.darpa.mil/Opportunities/SBIR_STTR/SBIR_STTR.aspx

Offerors responding to the DARPA topics listed in Section 8.0 of the DoD 12.B STTR Solicitation must follow all the instructions provided in the DoD Program Solicitation. Specific DARPA requirements in addition to or that deviate from the DoD Program Solicitation are provided below and reference the appropriate section of the DoD Solicitation.

SPECIFIC DARPA REQUIREMENTS:
Please note – these requirements and guidelines are supplemental to the DoD 12.B STTR Program Solicitation. For additional information, please refer to the corresponding section number in the DoD solicitation Preface).

2.3 Foreign National
DARPA topics are unclassified; however, the subject matter may be considered to be a "critical technology" and therefore subject to ITAR restrictions. ALL offerors proposing to use foreign nationals MUST follow Section 3.5, b, (8) of the DoD Program Solicitation and disclose this information regardless of whether the topic is subject to ITAR restrictions. See **Export Control** requirements below in Section 5.

3.5 Phase I Proposal Format
A Phase I Cost Proposal ($100,000 maximum) must be submitted in detail online via the DoD SBIR/STTR submission system. Proposers that participate in this solicitation must complete the Phase I Cost Proposal, not to exceed the maximum dollar amount of $100,000.

Offerors are REQUIRED to use the online cost proposal for Phase I costs (available on the DoD SBIR/STTR submission site). Additional details and explanations regarding the cost proposal may be uploaded as an appendix to the technical proposal. The Cost Proposal (and supporting documentation) DOES NOT count toward the 25-page limit for the Phase I proposal. Phase I awards and options are subject to the availability of funds.

**Please note: In accordance with section 3-209 of DOD 5500.7-R, Joint Ethics Regulation, letters from government personnel will NOT be considered during the evaluation process.

3.7 Phase II Proposals

DARPA Program Managers may invite Phase I performers to submit a Phase II proposal based upon the success of the Phase I contract to meet the technical goals of the topic, as well as the overall merit based upon the criteria in section 4.3 of the DoD Program Solicitation. Phase II proposals will be evaluated in accordance with the evaluation criteria provided in section 4.3. Information regarding Phase II Proposal format will be included in the Phase II Invitation letter.

In addition, each Phase II proposal must contain a five-page commercialization strategy as part of the technical proposal, addressing the following questions:

1. Product Description/System Application – Identify the Commercial product(s) and/or DoD system(s) or system(s) under development or potential new systems that this technology will be/or has the potential to be integrated into.

**2. Advocacy Letters – Feedback received from potential Commercial and/or DoD customers and other end-users regarding their interest in the technology to support their capability gaps.

**3. Letters of Intent/Commitment – Relationships established, feedback received, support and commitment for the technology with one or more of the following: Commercial customer, DoD PM/PEO, a Defense Prime, or vendor/supplier to the Primes and/or other vendors/suppliers identified as having a potential role in the integration of the technology into fielded systems/products or those under development.

4. Business Models/Procurement Mechanisms/Vehicles – Business models, procurement mechanisms, vehicles and, as relevant, commercial channels, and/or licensing/teaming agreements you plan to employ to sell into your targeted markets.

- What is the business model you plan to adopt to generate revenue from your innovation?
- Describe the procurement mechanisms, vehicles and channels you plan to employ to reach the targeted markets/customers.
- If you plan to pursue a licensing model, what is your plan to identify potential licensees?

5. Market/Customer Sets/Value Proposition – Describe the market and customer sets you propose to target, their size, and their key reasons they would consider procuring the technology.

- What is the current size of the broad market you plan to enter and the “niche” market opportunity you are addressing?
- What are the growth trends for the market and the key trends in the industry that you are planning to target?
- What features of your technology will allow you to provide a compelling value proposition?
- Have you validated the significance of these features and if not, how do you plan to validate?

6. Competition Assessment – Describe the competition in these markets/customer sets and your anticipated advantage (e.g., function, performance, price, quality, etc.)

7. Funding Requirements – List your targeted funding sources (e.g., federal, state and local, private (internal, loan, angel, venture capital, etc.) and your proposed plan and schedule to secure this funding. Provide anticipated funding requirements both during and after Phase II required to:

- mature the technology
- as required, mature the manufacturing processes
- test and evaluate the technology
- receive required certifications
- secure patents, or other protections of intellectual property
- manufacture the technology to bring the technology to market for use in operational environments
- market/sell technology to targeted customers

8. Sales Projections – Provide a schedule that outlines your anticipated sales projections and indicate when you anticipate breaking even.

9. Expertise/Qualifications of Team/Company Readiness - Describe the expertise and qualifications of your management, marketing/business development and technical team that will support the transition of the technology from the prototype to the commercial market and into operational environments. Has this team previously taken similar products/services to market? If the present team does not have this needed expertise, how do you intend to obtain it? What is the financial history and health of your company (e.g., availability of cash, profitability, revenue growth, etc)?

The commercialization strategy must also include a schedule showing the quantitative commercialization results from the Phase II project that your company expects to report in its Company Commercialization Report Updates one year after the start of Phase II, at the completion of Phase II, and after the completion of Phase II (i.e., amount of additional investment, sales revenue, etc. - see section 5.4).

**Please note: In accordance with section 3-209 of DOD 5500.7-R, Joint Ethics Regulation, letters from government personnel will NOT be considered during the evaluation process.

Phase II Proposal Format

A Phase II Cost Proposal ($1,000,000 maximum) must be submitted in detail online via the DoD SBIR/STTR submission system. Proposers that submit a Phase II proposal must complete the Phase II Cost Proposal, not to exceed the maximum dollar amount of $1,000,000.

Offerors are REQUIRED to use the online cost proposal for the Phase II costs (available on the DoD SBIR/STTR submission site). Additional details and explanations regarding the cost proposal may be uploaded as an appendix to the technical proposal. The Cost Proposal (and supporting documentation) DOES NOT count toward the 40-page limit for the Phase II proposal. Phase II awards are subject to the availability of funds.

If selected, the government may elect not to include the option in the negotiated contract.

4.0 Method of Selection and Evaluation Criteria

The offeror's attention is directed to the fact that non-Government advisors to the Government may review and provide support in proposal evaluations during source selection. Non-government advisors may have access to the offeror's proposals, may be utilized to review proposals, and may provide comments and recommendations to the Government's decision makers. These advisors will not establish final assessments of risk and will not rate or rank offeror's proposals. They are also expressly prohibited

from competing for DARPA SBIR or STTR awards in the SBIR/STTR topics they review and/or provide comments on to the Government. All advisors are required to comply with procurement integrity laws and are required to sign Non-Disclosure and Rules of Conduct/Conflict of Interest statements. Non-Government technical consultants/experts will not have access to proposals that are labeled by their proposers as "Government Only."

Please note that qualified advocacy letters will count towards the proposal page limit and will be evaluated towards criterion C. Advocacy letters are not required for Phase I or Phase II. Consistent with Section 3-209 of DoD 5500.7-R, Joint Ethics Regulation, which as a general rule prohibits endorsement and preferential treatment of a non-federal entity, product, service or enterprise by DoD or DoD employees in their official capacities, letters from government personnel will NOT be considered during the evaluation process.

A qualified advocacy letter is from a relevant commercial procuring organization(s) working with a DoD or other Federal entity, articulating their pull for the technology (i.e., what need the technology supports and why it is important to fund it), and possible commitment to provide additional funding and/or insert the technology in their acquisition/sustainment program. If submitted, the letter should be included as the last page of your technical upload. Advocacy letters which are faxed or e-mailed separately will NOT be considered.

4.2 Evaluation Criteria

In Phase I, DARPA will select proposals for funding based on the evaluation criteria contained in Section 4.2 of the DoD Program Solicitation, including potential benefit to DARPA, in assessing and selecting for award those proposals offering the best value to the Government.

In Phase II, DARPA will select proposals for funding based on the evaluation criteria contained in Section 4.3 of the Program Solicitation in assessing and selecting for award those proposals offering the best value to the Government.

As funding is limited, DARPA reserves the right to select and fund only those proposals considered to be of superior quality and highly relevant to the DARPA mission. As a result, DARPA may fund more than one proposal in a specific topic area if the quality of the proposals is deemed superior and are highly relevant to the DARPA mission, or it may not fund any proposals in a topic area. Each proposal submitted to DARPA must have a topic number and must be responsive to only one topic.

4.4 Assessing Commercial Potential of Proposals

DARPA is particularly interested in the potential transition of SBIR project results to the U.S. military, and expects explicit discussion of a transition vision in the commercialization strategy part of the proposal. That vision should include identification of the problem, need, or requirement in the Department of Defense that the SBIR project results would address; a description of how wide-spread and significant the problem, need, or requirement is; identification of the potential end-users (Army, Navy, Air Force, SOCOM, etc.) who would likely use the technology; and the operational environments and potential application area(s).

Technology commercialization and transition from Research and Development activities to fielded systems within the DoD is challenging. Phase I is the time to plan for and begin transition specific activities. The small business must convey an understanding of the transition path or paths to be established during the Phase I and II projects. That plan should include the Technology Readiness Level (TRL) at the start and end of the Phase II. The plan should also include a description of targeted operational environments and priority application areas for initial Phase III transition; potential Phase III transition funding sources; anticipated business model and identified commercial and federal partners the

SBIR company has identified to support transition activities. Also include key proposed milestones anticipated during Phase I, II or beyond Phase II that include, but are not limited to: prototype development, laboratory and systems testing, integration, testing in operational environment, and demonstrations.

5.1.b. Type of Funding Agreement (Phase I)

- DARPA Phase I awards will be Firm Fixed Price contracts.
- Companies that choose to collaborate with a University must highlight the research that is being performed by the University and verify that the work is FUNDAMENTAL RESEARCH.
- Companies are strongly encouraged to pursue implementing a government acceptable cost accounting system during the Phase I project to avoid delay in receiving a Phase II award. Visit www.dcaa.mil and download the "Information for Contractors" guide for more information.

5.1.c. Average Dollar Value of Awards (Phase I)

DARPA Phase I proposals **shall not exceed $100,000,** and are generally 6 months in duration.

5.2.b. Type of Funding Agreement (Phase II)

- DARPA Phase II awards are typically Cost-Plus-Fixed-Fee contracts; however, DARPA may choose to award a Firm Fixed Price Phase II contract or an Other Transaction (OT) on a case-by-case basis. Visit: http://www.darpa.mil/Opportunities/SBIR_STTR/Small_Business_OTs.aspx for more information on Other Transactions.
- Companies are advised to continue pursuit of implementation of a government acceptable cost accounting system in order to facilitate their eligibility for future government contracts.
- Companies that choose to collaborate with a university must highlight the research that is being performed by the university and verify that the work is FUNDAMENTAL RESEARCH.

5.2.c. Average Dollar Value of Awards (Phase II)

DARPA Phase II proposals should be structured as a 24 month effort in two equal increments of approximately $500,000 each. The entire Phase II base effort should generally not exceed $1,000,000.

5.3 Phase I Report

All DARPA Phase I and Phase II awardees are required to submit a final report, which is due within 60 days following completion of the technical period of performance and must be provided to the individuals identified in Exhibit A of the contract. Please contact your contracting officer immediately if your final report may be delayed.

5.11.r. Export Control

The following will apply to all projects with military or dual-use applications that develop beyond fundamental research (basic and applied research ordinarily published and shared broadly within the scientific community):

(1) The Contractor shall comply with all U. S. export control laws and regulations, including the International Traffic in Arms Regulations (ITAR), 22 CFR Parts 120 through 130, and the Export Administration Regulations (EAR), 15 CFR Parts 730 through 799, in the performance of this contract. In the absence of available license exemptions/exceptions, the Contractor shall be responsible for

obtaining the appropriate licenses or other approvals, if required, for exports of (including deemed exports) hardware, technical data, and software, or for the provision of technical assistance.

(2) The Contractor shall be responsible for obtaining export licenses, if required, before utilizing foreign persons in the performance of this contract, including instances where the work is to be performed on-site at any Government installation (whether in or outside the United States), where the foreign person will have access to export-controlled technologies, including technical data or software.

(3) The Contractor shall be responsible for all regulatory record keeping requirements associated with the use of licenses and license exemptions/exceptions.

(4) The Contractor shall be responsible for ensuring that the provisions of this clause apply to its subcontractors.

Please visit http://www.pmddtc.state.gov/regulations_laws/itar.html for more detailed information regarding ITAR requirements.

5.11.s. Publication Approval (Public Release)
NSDD 189 established the national policy for controlling the flow of scientific, technical, and engineering information produced in federally funded fundamental research at colleges, universities, and laboratories. The directive defines fundamental research as follows: "Fundamental research' means basic and applied research in science and engineering, the results of which ordinarily are published and shared broadly within the scientific community, as distinguished from proprietary research and from industrial development, design, production, and product utilization, the results of which ordinarily are restricted for proprietary or national security reasons."

It is DARPA's goal to eliminate pre-publication review and other restrictions on fundamental research except in those exceptional cases when it is in the best interest of national security. Please visit http://www.darpa.mil/NewsEvents/Public_Release_Center/Public_Release_Center.aspx for additional information and applicable publication approval procedures. Visit http://dtsn.darpa.mil/fundamentalresearch/ to verify whether or not your award has a pre-publication review requirement.

5.15.h. Human and/or Animal Use
This solicitation may contain topics that have been identified by the program manager as research involving Human and/or Animal Use. In accordance with DoD policy, human and/or animal subjects in research conducted or supported by DARPA shall be protected. Although these protocols will most likely not be needed to carry out the Phase I, significant lead time is required to prepare the documentation and obtain approval in order to avoid delay of the Phase II award. Please visit http://www.darpa.mil/Opportunities/SBIR_STTR/SBIR.aspx to review the Human and Animal Use PowerPoint presentation(s) to understand what is required to comply with human and/or animal protocols.

- **Human Use:** All research involving human subjects, to include use of human biological specimens and human data, selected for funding must comply with the federal regulations for human subject protection. Further, research involving human subjects that is conducted or supported by the DoD must comply with 32 CFR 219, *Protection of Human Subjects* http://www.access.gpo.gov/nara/cfr/waisidx_07/32cfr219_07.html) and DoD Directive 3216.02, *Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research* (http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf).

Institutions awarded funding for research involving human subjects must provide documentation of a current Assurance of Compliance with Federal regulations for human subject protection, for example a Department of Health and Human Services, Office of Human Research Protection Federal Wide Assurance (http://www.hhs.gov/ohrp). All institutions engaged in human subject research, to include subcontractors, must also have a valid Assurance. In addition, personnel involved in human subjects research must provide documentation of completing appropriate training for the protection of human subjects.

For all proposed research that will involve human subjects in the first year or phase of the project, the institution must provide evidence of or a plan for review by an Institutional Review Board (IRB) upon final proposal submission to DARPA. The IRB conducting the review must be the IRB identified on the institution's Assurance. The protocol, separate from the proposal, must include a detailed description of the research plan, study population, risks and benefits of study participation, recruitment and consent process, data collection, and data analysis. Consult the designated IRB for guidance on writing the protocol. The informed consent document must comply with federal regulations (32 CFR 219.116). A valid Assurance along with evidence of appropriate training for all investigators should accompany the protocol for review by the IRB.

In addition to a local IRB approval, a headquarters-level human subjects regulatory review and approval is required for all research conducted or supported by the DoD. The Army, Navy, or Air Force office responsible for managing the award can provide guidance and information about their component's headquarters-level review process. Note that confirmation of a current Assurance and appropriate human subjects protection training is required before headquarters-level approval can be issued.

The amount of time required to complete the IRB review/approval process may vary depending on the complexity of the research and/or the level of risk to study participants. Ample time should be allotted to complete the approval process. The IRB approval process can last between one to three months, followed by a DoD review that could last between three to six months. No DoD/DARPA funding can be used towards human subjects research until ALL approvals are granted.

- **Animal Use:** Any Recipient performing research, experimentation, or testing involving the use of animals shall comply with the rules on animal acquisition, transport, care, handling, and use in: (i) 9 CFR parts 1-4, Department of Agriculture rules that implement the Laboratory Animal Welfare Act of 1966, as amended, (7 U.S.C. 2131-2159); (ii) the guidelines described in National Institutes of Health Publication No. 86-23, "Guide for the Care and Use of Laboratory Animals"; (iii) DoD Directive 3216.01, "Use of Laboratory Animals in DoD Program."

  For submissions containing animal use, proposals should briefly describe plans for Institutional Animal Care and Use Committee (IACUC) review and approval. Animal studies in the program will be expected to comply with the PHS Policy on Humane Care and Use of Laboratory Animals, available at http://grants.nih.gov/grants/olaw/olaw.htm.

  All Recipients must receive approval by a DoD certified veterinarian, in addition to an IACUC approval. No animal studies may be conducted using DoD/DARPA funding until the USAMRMC Animal Care and Use Review Office (ACURO) or other appropriate DoD veterinary office(s) grant approval. As a part of this secondary review

process, the Recipient will be required to complete and submit an ACURO Animal Use Appendix, which may be found at: https://mrmc-www.army.mil/index.cfm?pageid=Research_Protections.acuro&rn=1.

6.3 Notification of Proposal Receipt

After the solicitation closing date, DARPA will send an e-mail to the person listed as the "Corporate Official" on the Proposal Coversheet with instructions for retrieving the letter acknowledging receipt of proposal from the DARPA SBIR/STTR Information Portal.

6.4 Information on Proposal Status

Once the source selection is complete, DARPA will send an email to the person listed as the "Corporate Official" on the Proposal Coversheet with instructions for retrieving letters of selection or non-selection from the DARPA SBIR/STTR Information Portal.

6.5 Debriefing of Unsuccessful Offerors

DARPA will provide debriefings to offerors in accordance with FAR Subpart 15.5. The notification letter referenced above in paragraph 6.4 will provide instructions for requesting a proposal debriefing. Small Businesses will receive a notification for each proposal submitted. Please read each notification carefully and note the proposal number and topic number referenced. All communication from the DARPA SBIR/STTR Program management will originate from the sbir@darpa.mil e-mail address. Please white-list this address in your company's spam filters to ensure timely receipt of communications from our office.

DARPA STTR 12.B Topic Index

DARPA STTR 12.B Topic Descriptions

ST12B-001 TITLE: Advanced Materials and Methods for Biospecimen Collection for Infectious Disease

TECHNOLOGY AREAS: Biomedical

OBJECTIVE: Develop advanced materials and technologies for swab or swab-like collection of biospecimens that can be used by a minimally-trained individual, can be shipped/stored under ambient conditions, and provide high efficiency recovery of analytes from the material. Desired technologies would advance methods to collect biospecimens, such as naso/oropharyngeal swabs, for the diagnosis of appropriate respiratory diseases. Developed swabs should be optimized for biospecimen collection and recovery with materials that maintain and preserve activity of viral or bacterial targets, while reducing the need for cold chain requirements (e.g., compatible with ambient temperature transport and storage). Swab designs that maintain sample collection efficiency, while decreasing the complexity or patient discomfort in the collection process are encouraged. Swabs should be compatible with standard clinical analytical methods in the centralized reference or biomedical research laboratory.

DESCRIPTION: Proper biospecimen collection is the most important step for a variety of healthcare applications including clinical diagnostics and biomedical research. In particular, swab-based collection is standard practice for recovery of pathogenic organisms responsible for infectious disease. The type of swab or collection material, the collection method, and the sample elution method may influence the detection of clinical analytes and may prevent proper clinical interpretation. 1-8

Several challenges exist with current swab-based biospecimen collection. For bacterial and viral cultures, the collected swab must often be placed in media to prevent drying and enable viability of fastidious organisms. Additionally, cold chain transport and storage may be required depending on the pathogen, and laboratory analysis must often be performed within 48 hours of collection. For DoD personnel in limited resource areas, the need for cold shipment, and a short window for analysis, severely limits access to clinical diagnostic tests. Improved swab materials could significantly improve accurate diagnosis of infectious diseases in deployed personnel.

Analyte recovery is also a current challenge. Recovery of analytes from swab collection material is highly variable (typically less than 50 % recovery) depending on the organism, collection matrix, transport/storage conditions, extraction technique, and analytical methods. This challenge is particularly limiting for clinical conditions where the analyte of interest in is very low abundance.

This effort seeks development of swab or swab-like materials and/or collection methods that are specifically designed for clinical applications such as infectious disease diagnostics. It is preferred that the direct collection technique is appropriate for biospecimens of interest for infectious disease detection and is applicable as a front-end for analysis in a clinical and/or research laboratory. Key attributes desired are: high efficiency collection, ease of use for collection, reproducibility of collection, and optimized analyte recovery for downstream analysis within a centralized reference or research laboratory environment. Maximized recovery and activity of nucleic acids, proteins, viable whole cells, active viruses, and bacteria is critical, especially for low abundance analytes. Materials of particular interest are those that preserve the analytes in the swab or in a secondary material without cold chain requirements (to include transport and storage) for >48 hrs, preferably for a week or longer.

Proposers may focus on the swab material and/or on optimization of buffers/materials for storage and/or recovery. Methods and materials of particular interest would ensure complete recovery of all captured analytes (including low abundance analytes), such as a dissolvable matrix that does not interfere with downstream analytical technologies, and permit the ambient temperature shipment followed by analysis, including cell culture, at a remote laboratory. Proposers are encouraged to consider methods and technologies compatible with Clinical Laboratory Improvement Amendment (CLIA)-waiver, good laboratory practices (GLP), and good manufacturing practice (GMP) procedures. Proposers may integrate a diagnostic test into device; however, collection, preservation, and recovery for the broadest clinical applications are desired.

PHASE I: Demonstrate feasibility of swab methods, materials, or integrated technologies. Proposers should address the quantitative advantages of the method compared to current commercially available swabs (see references), as well as the complete anticipated operating procedure for use to include direct biospecimen collection technique off an individual, swab drying time or secondary media introduction (if necessary), analyte (efficiency, function, and time), and compatibility with downstream analyses. Proposers should demonstrate initial designs and performance and project Phase II capabilities. Phase I efforts should justify the applicability to settings such as point of care and home use, and consideration of the U.S. Food & Drug Administration (FDA) regulations9 is encouraged.

PHASE II: Phase II efforts should quantify all performance parameters related to the stated objectives, including quantity of bio-specimen collected, recovery efficiency for various analyte types (nucleic acids, proteins, active virus, etc.), and performance with downstream assays. If sample preservation is pursued, performers should quantify recovery and analyte integrity following ambient temperature storage of known duration. Manufacturing designs and costs should be considered for all components of the device. Device potential for FDA clearance as a biospecimen collection device for home use or physician office use should be described.

PHASE III DUAL USE APPLICATIONS: The technology to be developed would enable reproducible biospecimen collection outside of a major clinical facility and therefore would have significant impact on the clinical diagnostic market and pharmaceutical research.

There is a significant commercial market for medical diagnostics, and home-use physician-office based diagnostic testing is a growing element of this market. The developed technology would allow collection and preservation of biospecimens in such settings and enable clinically valid diagnostic testing and remote clinical trials.

The technology to be developed is critical for DoD, as many medics have minimal training. Development of an FDA-approved biospecimen collection and storage device would enable reliable samples to be collected and shipped for analyses, even from patients located in remote/deployment settings. Potential customers include Military Health System - Defense Medical Research and Development Program (MHS DMRDP), Military Infectious Diseases Research Program (MIDRP), and Defense Threat Reduction Agency (DTRA).

REFERENCES:

1) J. Norris, K. Manning, S. Linke, J. Ferrance, and J. Landers. Expedited, Chemically Enhanced Sperm Cell Recovery from Cotton Swabs for Rape Kit Analysis. J. Forensic Sciences, 52 (4) 2007, 800-805.

2) Mulrennan S, Tempone SS, Ling ITW, Williams SH, Gan G-C, et al. 2010 Pandemic Influenza (H1N1) 2009 Pneumonia: CURB-65 Score for Predicting Severity and Nasopharyngeal Sampling for Diagnosis Are Unreliable. PLoS ONE 5(9): e12849.

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5) Joann L. Cloud, Weston Hymas, Karen C. Carroll. Impact of Nasopharyngeal Swab Types on Detection of Bordetella pertussis by PCR and Culture J Clin Microbiol. 40(10): 2002, 3838–3840.

6) Rose L, Jensen B, Peterson A, Banerjee SN, Arduino MJ. Swab materials and Bacillus anthracis spore recovery from nonporous surfaces. Emerg Infect Dis. 2004 June. Available from: http://wwwnc.cdc.gov/eid/article/10/6/03-0716.htm

7) Van Horn, K. G., Audette, C. D., Tucker, K. A., & Sebeck, D. (2008). Comparison of 3 swab transport systems for direct release and recovery of aerobic and anaerobic bacteria. Diagnostic Microbiology and Infectious Disease, 62(4), 471-473.

8) Tano E, Melhus A. Evaluation of three swab transport systems for the maintenance of clinically important bacteria in simulated mono- and polymicrobial samples. APMIS. 2011 Mar;119(3):198-203.

9) CLIA: http://wwwn.cdc.gov/clia/regs/toc.aspx

KEYWORDS: Swab, nasalpharnygeal, biospecimen, collection, preservation, point-of-care, home use, diagnostic

ST12B-002 TITLE: Forecasting Dynamic Group Behavior in Social Media

TECHNOLOGY AREAS: Information Systems, Human Systems

OBJECTIVE: Develop automated tools that can (1) learn models of the dynamics of inter- as well as intra- group interactions in social media and (2) track the evolution of such dynamics and derive causal factors from online interaction data.

DESCRIPTION: Social media have evolved from a platform that provides infrastructure that supports maintaining connections between friends to a platform that supports recruiting, collaborating, organizing, and competing for resources. Facebook has over 800M active users, 900M pages and groups, millions of new postings per day, and users are, on average, connected to 140 friends and 80 community pages. Many online communities enable the creation of virtual teams, which evolve over time. Among these communities and teams are terrorist and other criminal organizations.

Previous research studying community interactions in social media has had limited success. Clustering and community detection algorithms only find groups of closely collaborating individuals [1], and are unable to track the changing state of roles and interacting networks or model the causes of interactions between people and communities. The models developed to forecast online interactions are limited to person-to-person scientific collaborations [2] and longer-term connections to interest groups [3]. Social media interactions are much more dynamic. Some teams form, organize, perform activities, and dissolve quickly. Team members are often heterogeneous, performing different roles and activities online and in the physical world. The impact of these teams on the social landscape, their interactions with other teams, the evolution of network state over time, and competition with other teams and communities has not been adequately researched. Due to the overwhelming deluge of data generated by users across social media platforms, this analysis cannot be done manually.

One of the key insights from online collaboration research is that group dynamics are affected by many factors [4]. First, users often join the same group for varying reasons, possessing different knowledge, skills, and opinions, which affects their roles on the team and the interactions within the team. Second, interactions between groups and their members may result in changes to group structures and roles of individuals, producing mergers, switches and defections of the members to other teams. Finally, the teams' states and their activities evolve over time under influence of external factors. As people have limited resources to participate in online activities, their behaviors can be affected by team membership, motivating events, and shared knowledge. Many of these dynamics are due to the collaborative and competitive nature of online interactions. While collaborations in social media have been researched extensively, little attention has been paid to how the groups compete with each other for members and influence on opinions of other teams and communities. Understanding what affects such online behavior is needed for trend forecasting.

This topic seeks innovative research to develop automated tools that can (1) learn models of the dynamics of inter- as well as intra- group interaction in social media and (2) track the evolution of such dynamics and derive causal factors from online interaction data. The algorithms must be able to operate on large datasets of millions of nodes, generate robust and reliable group behavior and interaction models, and provide the users with factors and their relative contribution to changes in online behaviors. This technology will be used by analysts in forecasting online behaviors and identifying competition and possible cyber terrorism events.

PHASE I:

* Task 1: Design and prove the feasibility of a system that can track groups and their state changes in social media.
* Task 2: Research key indicators of group interactions, including competition, recruitment activities, and effects of events and topics on group structure changes.

PHASE II:
* Task 1: Design and develop a system that learns dynamics of group behavior and inter- and intra-group interactions in an unsupervised manner based upon design and innovation developed in Phase I.
* Task 2: Demonstrate the system on a social media dataset containing >1K groups, >100K postings/day, and >1M members. Achieve high accuracy (90%) of detecting group state changes, activities, conflicts, and competitions.

PHASE III DUAL USE APPLICATIONS: Successful development of the prototype capability would be of great interest to industrial espionage prevention specialists, law enforcement, market analysts, and polling organizations. This capability would be applicable to a broad range of tactical as well as strategic military operations.

REFERENCES:
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KEYWORDS: Machine learning, Social Networks, Social Media, Dynamics

ST12B-003 TITLE: Automated Approaches to Cellular Engineering and Biomanufacturing

TECHNOLOGY AREAS: Materials/Processes, Biomedical

OBJECTIVE: Develop an automated, software-controlled platform that enhances cutting edge methodologies for genome-scale cellular engineering to enable rapid engineering and optimization of new biomanufacturing systems.

DESCRIPTION: Current approaches to engineering biology rely on an ad hoc, laborious, trial-and-error process, wherein one successful project often does not translate to enabling subsequent new designs. As a result, the state of the art development cycle for engineering new biological products often takes several years and costs tens to hundreds of millions of dollars (e.g. microbial production of artemisinic acid for the treatment of malaria and the non-petroleum-based production 1,3-propanediol). The impact from these current approaches is that the number of new entrants and innovators into both the commercial and research space is immediately limited – few have the expertise, capital and/or time necessary to develop and engineer a new product. Consequently, while progress has been made, we are constrained to producing only a tiny fraction of the vast number of possible chemicals, materials, diagnostics, therapeutics, and fuels that would be enabled by the ability to truly engineer biology. A new approach is needed.

To address bottlenecks plaguing the biological design-build-test cycle and to enable more complex design and engineering, DARPA seeks technologies that enhance automation for genome-scale, cellular engineering. These include automated, programmable, affordable, and compact systems capable of running complex bio-engineering processes (e.g. genome engineering at multiple sites across the genome, cell transfection, combinatorial genome assembly, library design, continuous evolution, etc.). Successful approaches will leverage automation software to enable more complex and robust experimental design (e.g. real-time feedback and control) resulting in outcomes and a scale of experimentation that would be difficult to achieve otherwise.

Current platforms developed for complex, genome-scale, cellular engineering protocols are often custom-designed and tailored to a specific lab's expertise and needs. Few of these techniques are automated; the expectation being that others can implement the protocols in their own labs using their own, custom means. Consequently, transformative techniques are limited to the hands of a relative few. This underscores the inherent challenges to engineering biology – replicability and reproducibility. There is significant opportunity for the automation of complex cellular engineering, reducing variability between experiments, and increasing the throughput and capabilities of constructing new biological designs. These innovations will introduce new architectures and tools that will form the foundational technology for engineering biology.

This solicitation focuses on the development of automated platforms for enhanced, genome-scale, cellular engineering that enable rapid engineering and optimization of biotechnology, including new biologically-based manufacturing systems. Automated platforms should address several or all of the following challenges intrinsic to the dissemination of complex, cellular engineering protocols: reproducibility, replicability, robustness, efficiency of processes, throughput of experiments, and others. In addition, these automated platforms should enable new experimental protocols and designs that would be difficult or impossible to achieve otherwise (e.g. real-time feedback and control).

PHASE I: Develop an initial concept design for an automated platform for enhanced genome-scale cellular engineering that enables rapid engineering and optimization of new biomanufacturing systems. Develop detailed analysis of the automated platform's predicted performance, including detailed performance analyses of each of the component technologies and processes to be integrated. Include analysis of the performance compared to the standard, non-automated protocol and anticipated improvement on speed or complexity of process. Define key component technological milestones and metrics and establish the minimum performance goals necessary to achieve successful execution of the automated platform. Phase I deliverable will include both a technical analysis of the proposed platform and a commercialization assessment.

The technical analysis will include: a technical report of experiments supporting the feasibility of this approach; defined milestones and metrics (including minimum performance metrics) for the development and performance of component processes; a detailed design of the proposed automation platform system; and a description of new experimental protocols and designs that would be difficult or impossible to achieve without automation and software control (e.g. real-time feedback and control).

The commercialization assessment will include a Phase II proposal that outlines plans for the development, fabrication, and validation of an automated platform for genome-scale, cellular engineering. This proposal should also include a detailed assessment of the potential path to commercialization, barriers to market entry, competitive landscape (if it exists), and collaborators or partners identified as early adopters for the new system.

PHASE II: Finalize the design from Phase I and initiate construction and demonstration of a prototype of the automation platform. Demonstrate that each of the components and processes necessary for implementing the genome-scale, cellular engineering protocol are capable of being performed on an automated platform under software control.

Establish baseline performance metrics that improve on comparable non-automated and automated competing processes. Provide an experimentally validated performance comparison of the new, automated process to competing SOA processes. Key metrics include (but are not limited to): reproducibility of experiments, efficiency of component processes, throughput of experiments, total cost and total time to reach end goal, performance of final design/product, and amount of human intervention required.

Demonstrate new experimental protocols and designs that would be difficult or impossible to achieve otherwise (e.g. real-time feedback and control) and include attendant, relevant metrics of performance. Deliverables of a prototype device and valid test data appropriate for a commercial production path are expected.

PHASE III DUAL USE APPLICATIONS: The ability to rapidly engineer and optimize new biologically-based production systems will have widespread utility and applications across the entire biotechnology and pharmaceutical industries including rapid, optimized production of high value chemicals, industrial enzymes, fuels, diagnostics, and

therapeutics. These automated platforms would be impactful for industrial biotechnology firms as well as academic, research-scale operations.

These platforms could enable the DoD to leverage the unique and powerful attributes of biology to solve challenges associated with production of new materials, novel capabilities, fuels, and medicines while providing novel solutions and enhancements to military needs and capabilities. For example, automated genome-scale cellular engineering platforms will facilitate the design of systems to rapidly and dynamically prevent, seek out, identify, and repair corrosion/materials degradation—a challenge that costs the DoD $23B/yr and has no near term solution in sight.

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KEYWORDS: Bioengineering, Biomanufacturing, Biotechnology, Genomics, Synthetic Biology, Genetic Engineering, Biology, Molecular Biology, Automation, Robotics, Software, Microfluidics, Control Systems