QUESTIONS RESPONSES

QSP TOOLS SURVEY

Form description

Goals

1. Gain a comprehensive view of how organizations and individual scientists are implementing QSP modeling and how software tools are currently used by the QSP community for model-informed drug discovery and development (MID3)
2. Identify and prioritize software and modeling capabilities that are considered necessary for successful application of QSP modeling for MID3
3. Provide necessary information and feedback for software developers on how QSP software could be improved
4. Provide an objective evaluation of the capabilities of popular QSP modeling tools to inform the community

The emphasis is on tools and capabilities available now and what is expected in the future (within 3-year time frame)

INSTRUCTIONS

This survey consists of three sections. The first is GENERAL section in which questions relevant to user (and users' organizations) experience with QSP modeling are examined. The second is a TECHNICAL section in which software tools are evaluated by the user. The final section extends the technical evaluation into an opportunity to highlight PREFERRED FEATURES to be found in next-generation QSP software packages. The responses to the GENERAL section will be used to enhance and deepen the analysis of the TECHNICAL and PREFERRED FEATURES sections, and thus are equally important for the success of this survey. These three sections contain smaller subsections which are focused on more specific questions.

This survey is built as a series of questions with the option of selecting one or more answers. Please select a single item if empty circles are located next to possible answers. Please make single or multiple selections that apply if squares are located next to available choices. The selections you make should reflect your personal knowledge and experience with QSP modeling.

We value your time and effort. Completing the entire survey should take no more than 30-35 min; each section and subsection shows the approximate time to complete it. You have the choice to save the partially completed survey and continue next time. Although you may skip some sections we strongly encourage you to complete all of them.

Thank you!

To proceed please provide your name and e-mail. These will be used solely for the purposes of informing you about the results of the survey

Name (While optional we would recommend you provide your name and e-mail as a means for us to inform you about the results of the survey)

Short answer text

e-mail (Optional)

Short answer text

Section 2 of 5

1. GENERAL (5 min)

Describe your organization and your experience with QSP modeling

ABOUT YOUR ORGANIZATION (4 min)

Description (optional)

1.1 What best describes your organization (check one)?

- ○ Pharmaceutical or biotech company
- ○ CRO
- ○ Academia
- ○ Government institution including regulatory agencies
- ○ Non-profit organization
- ○ Other...

1.2 How large is your entire organization (check one)?

- ○ < 50 employees
- ○ 50-500 employees
- ○ 500-5,000 employees
- ○ > 5,000 employees

1.3 How do you best describe your current position/experience related to mathematical modeling for model-informed drug discovery and development (check all applicable)?

- [ ] QSP modeler
- [ ] PK/PBPK/DMPK modeler
- [ ] PKPD modeler
- [ ] Clinical pharmacologist that occasionally employs modeling (<50% effort)
- [ ] Other...

1.4 How do you best describe your experience with QSP modeling?

- ( ) No QSP experience
- ( ) End-User, interested primarily in the results of modeling and using existing QSP models
- ( ) Beginner-level modeler developing either small models or doing small modifications in existing models
- ( ) Intermediate level modeler, developing fit for purpose/project models
- ( ) Expert modeler developing large-scale modeling platforms for multiple projects and therapeutic areas
- ( ) Other...

1.5 What is your total experience in this (see above) and your previous roles related to QSP modeling?

- ( ) No experience
- ( ) Less than 1 year
- ( ) 1-3 years
- ( ) More than 3 years

THE FOLLOWING 6 QUESTIONS ARE RELATED TO YOUR SITE/DEPARTMENT (please focus where your knowledge is best)

Description (optional)

1.6 How large is your department (check one)?

- ◯ < 50 employees
- ◯ 50-500 employees
- ◯ 500-5,000 employees
- ◯ > 5,000 employees

1.7 How many scientists (users) are currently using QSP modeling research in your department directly through modeling work and QSP tool development?

- ◯ None
- ◯ 1-5 scientists
- ◯ 5-10 scientists
- ◯ More than 10 scientists

1.8 Currently how many scientists dedicate >50% of their effort to QSP modeling/research?

- ◯ None
- ◯ 1-5 scientists
- ◯ 5-10 scientists
- ◯ More than 10 scientists

1.9 Same question with <50% effort ?

- ◯ None
- ◯ 1-5 scientists
- ◯ 5-10 scientists
- ◯ More than 10 scientists

1.10 How many scientists do you expect in the next 3 years to be dedicated QSP modelers with >50% effort ?

- ○ None
- ○ 1-5 scientists
- ○ 5-10 scientists
- ○ More than 10 scientists

1.11 Same question with <50% effort ?

- ○ None
- ○ 1-5 scientists
- ○ 5-10 scientists
- ○ More than 10 scientists

1.12 How does your organization currently resource QSP modeling efforts?

- ○ No resources dedicated to QSP modeling
- ○ Rely on internal resources only
- ○ Outsource QSP modeling work
- ○ Combination of the above

1.13 In the model-informed drug discovery and development (MID3) process, where do you see QSP modeling producing substantial impact in your organization? (check all that apply)

- ☐ Go / no-go decision making
- ☐ Target prioritization
- ☐ Compound optimization and prioritization

- [ ] Prioritizing or evaluating combinations
- [ ] Market or competitor differentiation
- [ ] Therapeutic regimen evaluation
- [ ] Evaluating biomarkers and stratifying patients
- [ ] Safety/toxicology
- [ ] Preclinical phase (discovery)
- [ ] Translational phase – Phase 1 studies
- [ ] Early clinical – Phase 1 and 2 studies
- [ ] Late clinical – Phase 3 studies
- [ ] Other...

1.14 What are the current constraints/obstacles in promoting or expanding QSP modeling activities? (check all that apply):

- [ ] Lack of appropriate infrastructure
- [ ] Lack of scientists with appropriate expertise/experience
- [ ] Lack of management interest and/or support
- [ ] Budgetary limitations
- [ ] None of the above: no obstacles are foreseen
- [ ] Other...

DEVELOPING QSP MODELS (1 min)

Description (optional)

1.15 In your organization what types of QSP models are being developed and used? (check all that apply)

- [ ] Deterministic ODE based
- [ ] Deterministic PDE based (e.g. detailed spatial-temporal models)
- [ ] Agent based
- [ ] Stochastic
- [ ] Frameworks that employ combinations of the above models
- [ ] Other...

1.16 In QSP modeling, what are your near term (1 year) goals/deliverables? (check all that apply)

- [ ] Understanding biology and drug's mechanism of action
- [ ] Data analysis and parameter estimation
- [ ] Simulating clinical experiments/trials
- [ ] Optimization of experiments and/or clinical studies
- [ ] Simulating disease progression (short term/long term)
- [ ] Other...

After section 2 **Continue to next section**

Section 3 of 5

TECHNICAL (25 min)

Please select the software tool that you have most experience with and then evaluate it

SOFTWARE TOOL GRADED (choose 1) *

- ○ Berkeley MadonnaTM
- ○ JDesigner
- ○ Wolfram Systems Modeler
- ○ Mathworks SimBiology®
- ○ Matlab®
- ○ Bayer TC: PK-Sim®/Mobi®
- ○ R and R packages
- ○ Immunetrics Biosimulation Platform
- ○ NONMEM®
- ○ Entelos PhysioLab Modeler®
- ○ Monolix
- ○ Other...

After section 3 **Continue to next section**

Section 4 of 5

2. Technical (25 min)

The following questions are specific to the software you have selected from the above choices

OVERALL QSP SOFTWARE AND MODEL CAPABILITIES (4 Min)

Description (optional)

2.1 In which of the following functions does the software you've selected truly excel (your opinion):

- [ ] Model building/programming
- [ ] Running simulations
- [ ] Parameter estimation and data fitting
- [ ] Plotting/visualizing simulation results
- [ ] Statistical analysis of results
- [ ] Other...

2.2 Is software support for systems biology markup language (SBML) essential for your work?

- ( ) I know nothing about SBML
- ( ) I am not aware of SBML support by the software
- ( ) No, I don't use it
- ( ) Yes, it is essential for my work

2.3 Which operating systems do you use for your software tool?

- [ ] Microsoft Windows
- [ ] Linux

- [ ] MAC OS
- [ ] Other...

2.4 Do you use built-in/existing parallel simulation capabilities?

- ( ) I am not aware of such capabilities
- ( ) I do not use them
- ( ) Yes, I use them

2.5 What is your hardware architecture for running the software (check all that apply)?

- [ ] Laptop
- [ ] Workstation
- [ ] Cluster
- [ ] Cloud
- [ ] Other...

2.6 Do you use your tool to make standalone models/apps?

- ( ) Yes
- ( ) No
- ( ) I am not aware of that capability

2.7 Do you use software network/collaboration capabilities and version control within the tool to develop/run your models together with your colleagues?

- ( ) Yes
- ( ) No

- ( ) I am not aware of that capability
- ( ) No, I use an alternate version control software for this purpose

2.8 What type(s) of software deployment and IT support is used in your organization (department/site)?

- [ ] Standalone
- [ ] Centralized server based
- [ ] Web based

2.9 What types of models deployment do you use with your software tool? (select all that apply)

- [ ] Standalone
- [ ] Centralized server based
- [ ] Web based

2.10 Do you use software capabilities to export your models as a set of equations?

- ( ) Yes
- ( ) No
- ( ) I am not aware of that capability

2.11 What types of model do you develop/use with your software tool?

- [ ] Deterministic ODE based
- [ ] PDE based
- [ ] Statistical
- [ ] Agent based

- [ ] Stochastic
- [ ] Other...

SOFTWARE TOOL(S) MODEL DEVELOPMENT CAPABILITIES (3 min)

Description (optional)

2.12 Do you use a graphical user interface (GUI) for visual (by using diagrams) model design and quick prototyping?

- ( ) I prefer not to use GUI
- ( ) I prefer to use GUI but it is not available
- ( ) I try to use as many GUI capabilities as possible

2.13 Is having a model debugging capability important in your work?

- ( ) No, I am not using it
- ( ) Yes, but I don't use it often
- ( ) Yes, it is very important and I use it routinely
- ( ) Yes, it is very important, but it is not available in this tool

2.14 In your model development do you use the scripting features supported by the platform to expand its capabilities?

- ( ) I do not use scripting
- ( ) Yes, I employ it in a limited way
- ( ) Yes, I extensively use software scripting tools
- ( ) Yes, I extensively use scripting but in a different platform

2.15 Does the software offer adequate scripting capabilities, language(s) and scripting editor?

- ○ Yes, I find both of them adequate
- ○ I would like to have a more comprehensive scripting language
- ○ Would like to have a more capable text editor
- ○ Both need improvement
- ○ I do not use scripting

2.16 Do you find capabilities used for model documenting, including literature references, HTML support, etc., adequate?

- ○ I am not aware of model documenting capabilities
- ○ I prefer to document my model using other resources
- ○ I would like to have better documenting capabilities
- ○ I find documenting capabilities adequate

2.17 With the tool are you able to use existing models as building blocks (modularity)?

- ○ I am not aware of that capability
- ○ I rarely use since this requires extensive work
- ○ I regularly use this capability

2.18 Do you use/need software capability for replicating modules/biology (e.g., representing multiple cells of the same type) and support for object-oriented design?

- ○ No, I don't use it and I don't need it
- ○ I don't use it because it is not available

- ○ I use it, but I want to have more capabilities
- ○ I use it and find provided capabilities adequate

PARAMETER ORGANIZATION (1 min)

Description (optional)

2.19 Do you find the way parameters are organized, especially for larger models, convenient and easy to work with?

- ○ Not organized
- ○ Organized but with limited features
- ○ Organized in a flexible structure with powerful handling tools/features

2.20 Do you use parameter manipulation and parameter export/import to/from different software (Excel, database, etc.)?

- ○ I am not aware of that capability
- ○ I use export/import, but options are limited
- ○ I find export/import capabilities adequate
- ○ I don't use export/import, since parameter manipulations provided by the software are adequate

PARAMETER ESTIMATION (2 min)

Description (optional)

2.21 Do you find parameter estimation capabilities provided by the software sufficient?

- ○ I am not aware of that capability
- ○ I feel that capabilities are very limited
- ○ Existing capabilities are sufficient

2.22 Do you use the software for parameter sensitivity analysis?

- ○ No
- ○ I am not aware of that capability
- ○ Yes, but software provides very limited capabilities
- ○ Yes, and I am satisfied with existing capabilities

2.23 What parameter estimation methods do you use most often?

- ☐ I am not aware of that capability
- ☐ Nonlinear mixed effects modeling
- ☐ Gradient algorithms
- ☐ Simplex algorithms
- ☐ Global optimization algorithms (e.g., genetic algorithm)
- ☐ I don't use parameter estimation
- ☐ Other...

2.24 What kind of data do you use with the software platform for the purposes of parameter estimation and/or model qualification?

- ○ I am not aware of that capability
- ○ Simple data sources (statistics, mean time courses, etc.)
- ○ Rich data sources (individual-level time courses, bioinformations/omics data, etc)

NUMERICAL SOLVERS (1 min)

Description (optional)

2.25 Are the numerical solvers/algorithms provided by the software adequate for your work?

- ○ Yes, I am satisfied with the options
- ○ No, the options are limited
- ○ No selection, only one method is supplied

2.26 If you want to add more solvers, which one would you select?

- ☐ Fixed step
- ☐ Adaptive step
- ☐ Stiff, not CVODE/LSODA
- ☐ CVODE/LSODA
- ☐ Stochastic simulation (Gillespie) algorithm
- ☐ Fixed point solvers (linear and nonlinear)
- ☐ Other
- ☐ N/A, I am satisfied with the solver options

VISUALIZATION AND DATA ANALYSIS (1 min)

Description (optional)

2.27 With the software you use how do you perceive the speed/ease of plotting/presenting simulation results?

- ○ Plotting capabilities are absent or very limited
- ○ Requires a lot of repetitive work
- ○ Easy and simple but wish to be more flexible
- ○ Highly customizable, meets all my needs

2.28 What features of the software do you value most for data plotting/visualization?

- [ ] Ability to quickly visualize the results by using prebuilt plot templates
- [ ] Large selection of visualization/plot types
- [ ] High flexibility to make custom plots
- [ ] Ability to overlay simulation results with external data
- [ ] I do most of my plotting with a different software

2.29 Do you employ statistical analysis tools provided by the software?

- ( ) I don't use statistical methods in my data analysis
- ( ) Yes, I use them but the selection is limited
- ( ) Yes, and I find all the tools I need
- ( ) No, I find using specialized statistical tools more attractive

2.30 Do you find the software's capabilities to export simulation results into other formats for outside manipulation/analysis adequate?

- ( ) I am not aware of that capability
- ( ) I export results as simple text (tab, csv)
- ( ) I export results as spreadsheet or data analysis proprietary format (excel, SAS)
- ( ) I use direct upload to database for future queries

SUPPORT FOR RUNNING EXPERIMENTS, CREATING VIRTUAL PATIENTS AND VIRTUAL POPULATION (1 min)

Running simulations with different sets of parameters could be considered as running virtual experiments. If such parameters represent variations in biological/physiological behaviors, these alternative virtual experiments could be viewed as different Virtual Patients (VPs). Collections of VPs that model clinical populations could be considered as Virtual Populations (VPops)

2.31 Do you employ the software for creating VPs and VPops?

- ○ I don't create/use the concept of VPs and VPops
- ○ I am not aware of any tool for creating VPs and/or VPops
- ○ I use the software for creating VPs and/or Vpops, but the capabilities are limited
- ○ This software covers all my needs in either VP or/and Vpops development and running virtual experiments

2.32 Do you find organization/structure of experiments, VPs, and VPops adequate and useful for running simulations with multiple experiments and/or VPs and VPops?

- ○ I am not aware of any such feature or tool
- ○ I find existing capabilities limited and not easily scalable
- ○ I find existing capabilities flexible, scalable, and easy to use

SOFTWARE COST (1 min)

Description (optional)

2.33 Does the cost of the software ownership, including the cost of the license, add-on packages, and/or customer support and annual maintenance fees play an important/definitive role in your decision to use/not use it?

- ○ Yes, with no budgetary constraints I'd definitely use a different software tool
- ○ Yes, it plays important but not decisive role
- ○ No, cost does not play decisive role, software capabilities do

AVAILABLE QSP MODELS AND SOFTWARE CUSTOMER SUPPORT (2 min)

Description (optional)

2.34 Do you find the software customer support adequate and useful?

- ○ I am not aware of customer support or it is not provided
- ○ I find it somewhat useful

- ○ I find it very helpful most of the time

2.35 What other sources of information about the software do you use?

- ☐ Software community forums
- ☐ Software documentation and help system
- ☐ Peer-to-peer communications
- ☐ On-line resources (tutorials, video, etc.)

2.36 Are you using existing QSP models/model platforms (including freely available) with your software?

- ○ I am not aware of existing models
- ○ I don't find existing models very useful
- ○ I don't use existing models/platforms since they are expensive
- ○ I am using existing models

After section 4 **Continue to next section**

Section 5 of 5

3. PREFERRED FEATURES (4 min)

In order to develop better and more useful QSP software tools it is essential to understand what features in the tools are considered most important. You have an opportunity to rank the software features listed below depending on how important are they for your work. Please assign a rank from the following selection, 1 "least important", 2 "somewhat important" , 3 “most important” to each feature. Try to spread your choices evenly between these three selections, ideally each rank should be assigned 6 times.

3.1 Ability to easily develop and simulate large (>20 state variable) models

	1	2	3	
Least Important	○	○	○	Most Important

3.2 Support for SBML export or export to any other widely used language (R, Matlab, Python, etc)

	1	2	3	
Least Important	○	○	○	Most Important

3.3 High-performance parallel computing enabled

	1	2	3	
Least Important	○	○	○	Most Important

3.4 Support for flexible hardware architecture (e.g., standalone computer, cluster, cloud, network) and computational environment (multiple operating systems)

	1	2	3	
Least Important	○	○	○	Most Important

3.5 Availability of multiple numerical solvers

	1	2	3	
Least Important	○	○	○	Most Important

3.6 Support for scripting tasks that extend the tool's capabilities

	1	2	3	
Least Important	○	○	○	Most Important

3.7 Support for multiple parameter estimation algorithms

	1	2	3	
Least Important	○	○	○	Most Important

3.8 Ability to store and handle a large number of parameters in a structured way, including parameter export/import

	1	2	3	
Least Important	○	○	○	Most Important

3.9 Visual diagrammatic model creation/editing capability (in contrast to purely text-based model development)

	1	2	3	
Least Important	○	○	○	Most Important

3.10 Modular (plug-and-play) model architecture

	1	2	3	
Least Important	○	○	○	Most Important

3.11 Support for easy creation of replicated features (e.g., array of cells, array of similar compounds, etc.)

	1	2	3	
Least Important	○	○	○	Most Important

3.12 Built-in support for easy and flexible visualization of simulation results

	1	2	3	
Least Important	○	○	○	Most Important

3.13 Availability of tools for Virtual Patients (VP) and Virtual Populations (VPops) creation

	1	2	3	
Least Important	○	○	○	Most Important

3.14 Support for VPops manipulation, sampling, and clinical trial simulation

	1	2	3	
Least Important	○	○	○	Most Important

3.15 Low cost of ownership and maintenance

	1	2	3	
Least Important	○	○	○	Most Important

3.16 Customer support

	1	2	3	
Least Important	○	○	○	Most Important

3.17 Selection of disease models (platforms) already available for this particular software

	1	2	3	
Least Important	○	○	○	Most Important

3.18 Integration with additional external tools, e.g., bioinformatics

	1	2	3	
Least Important	○	○	○	Most Important

Feel free to add comments on the tools, features not mentioned, features you would like to have, and survey itself in the box below. THANK YOU !

Long answer text