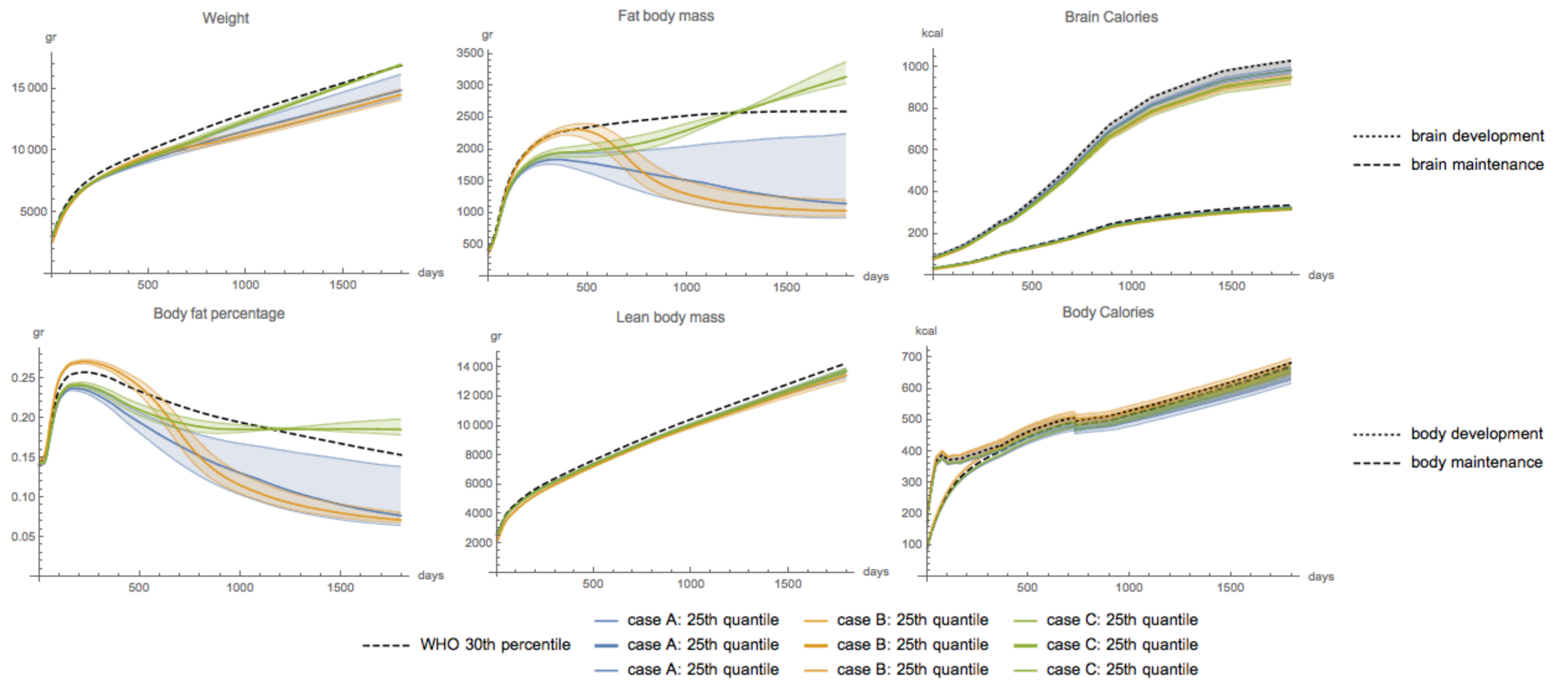


Competitive Body and Brain Growth Model

Jason Cawley,^a Filippo Visco-Comandini,^a Onkar Singh,^a Marco Guidetti,^a Representing the Healthy Birth, Growth, and Development knowledge integration (HBGD*ki*) Community^b

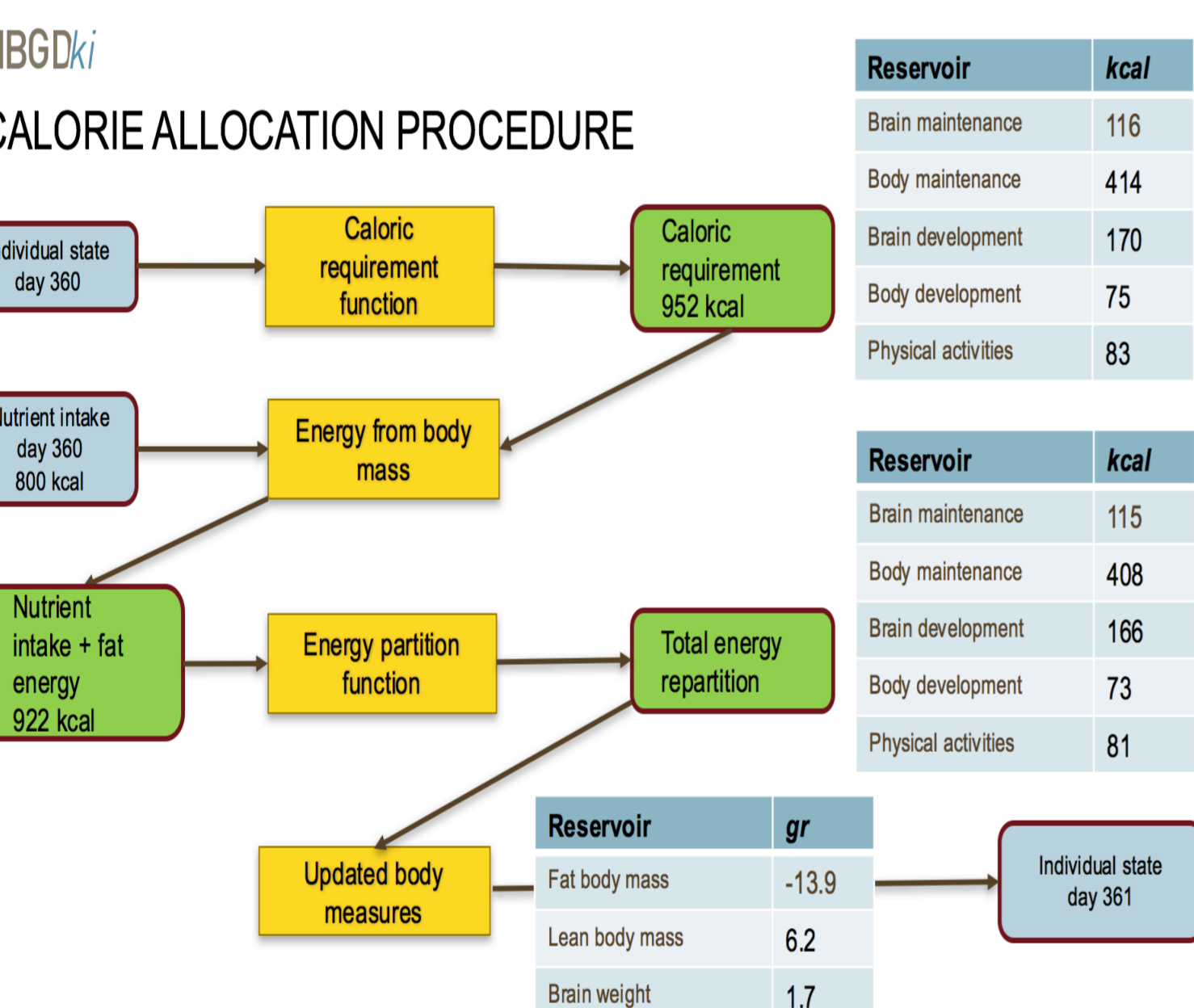
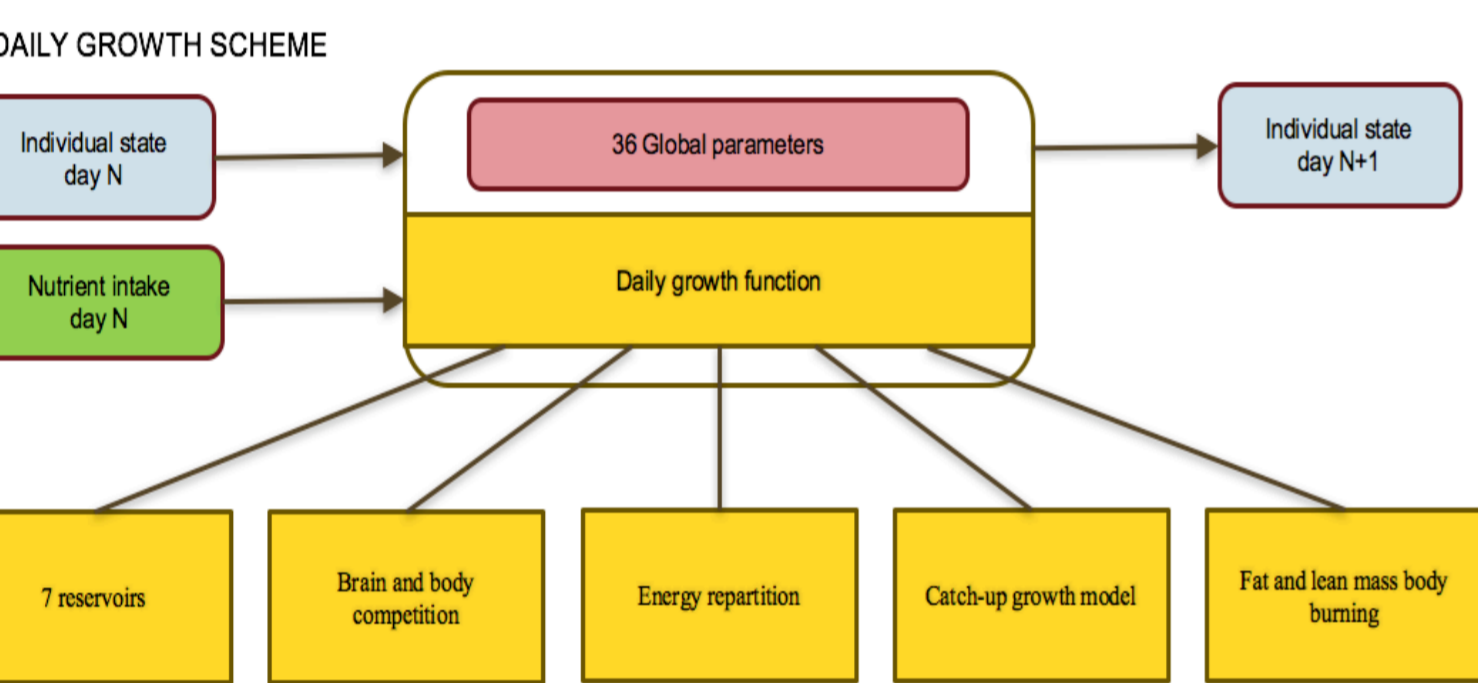
^aWolfram Solutions, Champaign, IL, USA; ^bBill & Melinda Gates Foundation, Seattle, WA, USA

----	30th percentile WHO Standard growth track
—	case A involves a male child with a birth weight of 3000 gr with the 95% of the regular feeding of the 30th percentile of WHO standard growth track from day 1.
—	case B is the same as case A except he has competition parameters that sacrifice brain development before body development and physical activity.
—	case C involves a male child with a birth weight of 2500 gr instead of 3000 gr who was fed 100% of the regular feeding of the 30th percentile of the WHO standard growth track for the first year, and from day 360 was fed with 95% of that amount. Uses the same competition parameters as case A. Shaded regions reflect 50% confidence interval for population variation



Objective

- To model the resource competition between body and brain during human development from birth to age 5 y in nutritionally challenged populations.



days	weight	height	lean body mass	fat body mass	body fat percentage
1	0.14	0.14	98	0.14	98
180	0.26	0.24	93	0.24	94
359	0.25	0.22	88	0.23	91
538	0.23	0.19	82	0.21	89
717	0.21	0.16	77	0.19	90
896	0.20	0.14	71	0.19	93
1075	0.19	0.12	65	0.19	98
1254	0.18	0.11	60	0.19	103
1433	0.17	0.09	55	0.19	109
1612	0.16	0.08	52	0.19	115
1791	0.15	0.08	50	0.19	121

days	WHO 30 percentile data (g)	case A (g)	case A %	case B (g)	case B %	case C (g)	case C %
1	2630.67	2580.89	98	2580.89	98	2150.74	82
180	5546.57	5352.14	96	5352.37	96	5097.40	92
359	6804.59	6559.53	96	6559.91	96	6373.71	94
538	7804.85	7616.35	96	7617.09	96	7474.55	95
717	8943.96	8616.35	96	8616.45	96	8498.83	95
896	9933.64	9567.44	96	9568.80	96	9446.05	95
1075	10823.30	10423.90	96	10425.80	96	10284.30	95
1254	11690.70	11258.80	96	11261.70	96	11096.30	95
1433	12549.40	12083.30	96	12089.60	96	11890.60	95
1612	13405.30	12898.80	96	12914.70	96	12667.30	94
1791	14253.80	13696.10	96	13732.80	96	13420.90	94

days	WHO 30 percentile data (kcal)	case A (kcal)	case A %	case B (kcal)	case B %	case C (kcal)	case C %
1	54.28	50.58	93	50.45	93	47.55	88
180	98.17	92.85	95	89.12	91	89.63	91
359	155.79	147.92	95	142.40	91	145.70	94
538	245.43	232.42	95	222.72	91	228.73	93
717	363.51	344.37	95	330.16	91	333.46	92
896	482.82	457.90	95	438.72	91	440.80	91
1075	584.28	535.98	92	513.02	88	514.19	88
1254	612.99	582.45	95	557.39	91	558.98	91
1433	697.80	624.99	90	598.18	86	600.42	86
1612	877.38	844.05	96	816.16	93	818.95	93
1791	993.02	959.32	97	930.70	94	933.67	94

Methods

- The competitive brain and body growth model computed growth trajectory for a single subject, and included daily nutrient intake.
- The model was a recursion of a daily growth function, that took as input the individual state and nutrient intake for a particular day.
- The model returned the new individual state for the next day.
- Energy use was tracked across multiple reservoirs: basal metabolism for between brain and body maintenance², activity, brain growth^{3,4}, lean body mass growth, and fat use or accumulation.
- Several global parameters were important in model behavior and were modified to adjust model predictions or performance.
- These parameters included competition coefficients that encoded the relative priority of different uses of available energy when overall energy was constrained.
- The model used discrete time steps (not continuous differential equations).
- A single time step – typically 1 d – took a subject from one to a new state; all reservoirs were updated and various necessary measures were computed along the way.
- The model evolved by repeating the application of the single step.
- At each step, new input parameters specific to that step were added, such as daily caloric intake.
- The expected growth at each age also was used in each step, so each time step differed from previous steps.

Results

- Normative growth curves associated with each percentile growth channel of the World Health Organization standard growth curves¹ were characterized.
- The model estimated daily nutrient intakes for the first 5 years of a longitudinal Guatemala study (92 children).
- The model estimated the approximate path of nutrient intake received by each subject, to fit a set of known weights at reported times.
- The full nutrient intake path had more degrees of freedom than number of known weights; therefore, we sought an average level of feeding relative to the subject's estimated caloric needs in a piecewise fashion, from one measurement to the next.
- The fitting procedure was promising but did not have unique solutions.
- It was determined that more data sets would be needed to narrow the parameter space, including plausible feeding scenarios for healthy and challenged populations and basic growth phenotypes.

References

- WHO growth charts. National Center for Health Statistics. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/growthcharts/>. Accessed May 18, 2016.
- Butte NF. Energy requirements of infants. *Public Health Nutr.* 2005;8(7A):953-967.
- Dekaban AS. Changes in brain weights during the span of human life: relation of brain weights to body heights and body weights. *Ann Neurol.* 1978;4(4):345-356.
- Kuzawa CW, et al. Metabolic costs and evolutionary implications of human brain development. *Proc Natl Acad Sci U S A.* 2014;111(36):13010-13015.

Conclusions

- The competitive body and brain model may provide a framework for mechanistic exploration of anthropometric outcomes and permit evaluation of different scenarios of nutrient intake, such as regular feeding, malnutrition, and caloric intake to support catch-up growth.
- The model characterized normative infant growth curves and simulated different scenarios including regular feeding, catch-up growth, and under- and over nutrition based on changes in nutritional intake.
- Available energy generated from varied nutrient intake was assigned to different reservoirs that may compete for caloric resources when there is underfeeding and malnutrition.

Acknowledgements

Thanks to the Bill & Melinda Gates Foundation and Shasha Jumble for inspiration and direction on this project.

We thank Thomas Peyret, Rukmini Kumar, and Lyn Powell for useful feedback and discussion.